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THE CHEMICAL MANIPULATION OF FOOD*

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The object of this lecture is to call attention to the great expansion and development of the treatment of food, during processing and production, by chemical substances foreign to the body. There are indications that this subject is now an important problem of public health, and unless controlled and wisely guided this practice may have a detrimental effect on the health of the country. It is particularly important that medical men should appreciate what is happening, for whatever is done to food ought to be dominated and decided by its effect on human health. It seems that the ordinary consumer often appreciates the changes in the aesthetic value of the food so treated even though such treatment may either lower its nutritional value or, in some cases, produce a toxic product. The consumer must be protected against himself and against the wayward choices of food into which his appetite leads him.

As matters stand at present the chemist holds the dominant position in developing and controlling the subject, and the great expansion of food manipulation is an indication both of his energy and of his success in this field of action. Chemists primarily engaged in this work are called "food scientists," a designation which is misleading, because they often have but little knowledge of the physiology and pathology of the animal body, nor do they in general grasp the significance or the difficulties and complexities of living processes. They are apt to view the reactions of the human body from the point of view of chemistry—a subject which is so highly developed, and so often lends itself to correct prophecy, that other scientific implications seem relatively easy. But the fact is that actions and reactions of the human body are so unpredictable, and knowledge of them so meagre, that the confidence and clear-cut views of the chemist may often be dangerous. That is why, if this subject is allowed to develop, medical scientists must play a leading part, especially before official decisions are made on the adoption and rejection of processes of chemical manipulation of food.

Present Practice

At the present time, both in the U.S.A. and in this country, it is possible for chemical substances to be used in food manipulation and production which ultimately prove to be harmful and deleterious. This does not mean that substances known to be harmful can be added to food but only that chemicals are often assumed to be harmless and, after being used for a longer or shorter time, are then proved to have harmful properties. This kind of incident is constantly happening. It was stated at a recent inquiry in the U.S.A. that of 700 chemical agents at present used in food preparation 246 had not been studied enough from a toxicological angle to satisfy the Food and Drug Administration of that country that they were innocuous. Even when such chemical substances have passed through a battery of tests from the point of view of toxicology, unexpected harmful results have often ultimately been demonstrated.

Medical science often cannot give adequate answers to questions of toxicological action, not only as regards new compounds but even in the case of substances long in use. Indeed, to the medical man unpleasant surprises are constantly being revealed, in the case both of drugs and of chemicals used in food preparation. Many instances of such occurrences could be given, but two, in relation to drug action, which will be known to many medical men will be mentioned.

A series of cases of agranulocytosis often associated with septic throats (Vincent's angina) came to light about 1935–9 in which the individuals affected were found to have taken a well-known and extensively advertised patent medicine. The cause of the trouble in these cases was traced to the amidopyrine present in the patent remedy. As soon as the discovery was made and announced, many further instances turned up, and indeed a number of other chemical substances were later discovered to have a similar toxic action. This was a surprising poisonous action of a drug which had been long in use.

Another similar unexpected result casually observed quite recently has been the discovery that resorcinol, which has been a long-standing remedy as an antiseptic in skin disease, has the remarkable effect in some people of producing myxoedema and enlarged thyroid (Bull and Fraser, 1950).

It can be easily understood how these harmful effects have escaped detection by systematic toxicological inquiry in the past; but each discovery of the kind leads to an improvement in the technique of toxicology, and it is upon the still greater development of this subject that reliance must be made.

In this country there seems to be a special difficulty in controlling the situation, because the use of chemicals in food preparation is largely decided by the Ministries of Food and of Agriculture and Fisheries, whose main objectives must be the production of foodstuffs which are more abundant and acceptable to the consumer. It is undoubted that these Ministries also take into consideration the possible effects on the health of the consumer, but this aspect does not hold the commanding position that it clearly should. With the best will in the world these Ministries cannot, without the guidance of medical science, decide with knowledge and wisdom such questions affecting health. The duty of considering

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health officially devolves primarily upon the Minister of Health, and it would be more comforting if it were clear that all questions involving the addition of unnatural chemicals to food were more controlled and even dependent upon the decisions of that Minister.

Conditions in the U.S.A.

At the present time in the U.S.A. both Government Departments and the general public are keenly alive to the dangers of the position. The Food and Drug Administration has extensive laboratories and a large research staff engaged in the work, and official inquiries of a high legal and scientific standard are often held on specific matters of interest. At these inquiries experts are not encouraged to give their opinions only, but definite evidence on each point must be presented and filed as exhibits, so that the presiding officer can carefully examine and balance the evidence before coming to a decision.

We seem to have no such highly developed laboratory and examining mechanism in this country, and we are in the undignified position of having often to rely on the decisions arrived at in the U.S.A. before policy or action can be determined. If the questions at issue were small and of rare occurrence this situation might perhaps be regarded with more complacency, but this is not the case. Questions of great public interest are constantly cropping up, and the food and drug laboratories in America are very active. Is it right, therefore, that we should continue to be onlookers in this field of action, profiting by and dependent upon the hard work and the keen interest of another country? A beginning has been made here by the establishment of a toxicological research unit by the Medical Research Council, but this is far too small for work of the proposed type; and its objects are different from those of an officially developed testing department such as the Food and Drug Administration of the U.S.A.

It is of course true that in this field, as in most fields of scientific research, important contributions are sometimes made to the subject by private investigations here—such, for instance, as the carcinogenic properties of organic compounds of the coal-tar type and especially of the azo dyes—but, whereas we often look on such contributions with passive equanimity, the U.S.A. seize on each discovery and by much labour apply it to the practical problems of food adulteration in relation to public health. Equally, their food manufacturers quickly and vigorously apply any new knowledge of chemical manipulation to the development of their products.

There is no question of apportioning blame in this problem. Food manufacturers and scientists, as well as official bodies, are undoubtedly anxious to do the right thing, and the question really resolves itself into the adoption of the best methods of dealing with the situation and the right angle at which to survey such problems. An enlightened public guided by good leadership, medical and scientific, will form the essential basis for proper action in such matters.

Changes in Disease Incidence

It may be asked if changes in the incidence of disease, especially in the past 50 years, afford any reason for suspecting that the modern practice of chemical manipulation of food is having any harmful effects on health. This is not easy to answer, for there is nothing more difficult than guessing and forecasting in biological and medical problems, and in the present situation there are many unknown factors. Although most morbid conditions have rapidly diminished in highly developed Western countries in the present century there are a number which have increased, and this increase cannot wholly be explained on the basis of an ageing population. It is difficult to avoid the conclusion that some at least of these increases in disease are due to errors in living recently introduced or greatly expanded in modern times.

The present popular explanation of some is that they are largely of a psychosomatic origin, due to the modern stress of life. Such an explanation leaves the problems in the air from a research angle. Is this explanation sufficient to account for the great increase in abdominal trouble, and especially of gastric and duodenal ulcers, cholecystitis, and appendicitis? There are also diseases, fairly common in incidence, like hypertension, the leukaemias, and disseminated sclerosis, the aetiology of which has defied all investigation. The great increase in diabetes in modern times in the U.S.A., and in this country until the recent war, is also still an unsolved problem.

In most of these diseases there are great differences in incidence in different countries. For instance, there is almost a complete absence of disseminated sclerosis among the South-African-born white population, and the incidence of the above-mentioned alimentary disorders among the natives of tropical and subtropical countries is much smaller than in Western Europe and America. There is therefore good reason to believe that much disease in Western countries at present is due to errors of living introduced or greatly increased in modern times, and it may be that one of these errors is the ingestion of food treated by unnatural chemical substances. It is at least a subject worthy of inquiry, and might well be considered whenever a disease commonly found in countries which use these methods has resisted all efforts of the investigator to find a satisfactory aetiological basis.

There are therefore two main problems presented by this modern development of food processing and production affecting the consumer. One, the possibility of the introduction into food of substances which confer upon it toxic properties; and, secondly, the degradation of the nutritional qualities of food by the abstraction or reduction of some of its important constituents or by the dilution of its nutritional constituents by air and water. Of these two problems the second may be more difficult to combat.

Chemicals Used in Food Preparation and Production

Unnatural chemicals are used in food preparation and production for the following main purposes: (1) added to foodstuffs as fat-sparers (extenders) or sparers of other foods, to facilitate emulsification and as preservatives, antioxidants, sweetening, flavouring, and colouring agents, and as improvers and bleachers of flour; (2) to aid in the washing of utensils used in food production, processing, and wrapping; (3) as wax coatings, resins, plasticizers, and other ingredients of food-packing material; and (4) as pesticides, including insecticides, fungicides, acaricides, herbicides, and plant-growth regulators in the production of fruit and vegetables.

Let us now briefly examine some of the chemical agents used for the above purposes. In the first place I shall deal with the evidence which shows that some of these substances, a number of which have long been in extensive use, are harmful to animals. As regards the toxic action of these adulterants it is obvious that if substances can be shown with certainty to have bad effects they are unlikely to continue in permanent use. This question of degree of toxicity is often difficult to decide, and instances will be mentioned in which the use of substances has continued and is continuing although there is evidence that they are harmful, because such evidence or deductions made therefrom are not unanimously accepted.

Sweetening Agents

One of the simplest instances of chemicals used in food preparation is that of sweetening agents. These substances are valuable as substitutes for sugar in the diet of diabetics, but are also extensively used for normal consumption in the soft-drink industry and in baking and in the manufacture of confectionery. Of these, four compounds have been used: (1) saccharin, (2) dulcin, (3) P 4,000, and (4) sodium cyclohexylsulphamate. These substances have been tested from the point of view of chronic toxicity by Fitzhugh and Nelson (1950), and interesting and unexpected results have come to light.

Dulcin (paraphenetolurea) had been used as a sweetening agent for 50 years before the chronic toxicity tests on animals showed it to be harmful. In animals fed at dosage levels of 0.1% and above, large liver tumours were produced. At higher levels of feeding (0.5–1%) growth was retarded and the mortality rate increased. At 1% the blood picture became abnormal, including a reduction in the red-cell count and the appearance of normoblasts. P 4,000 (2-amino-4-nitrophenylpropyl-ether), which received its descriptive name because it has about 4,000 times the sweetening power of cane sugar, was first reported from Holland as non-toxic. It is, however, a local anaesthetic as well as a sweetening agent, and has recently been shown to produce pigment changes in the thyroid gland and kidney damage (Fitzhugh and Nelson, 1950). Under the same experimental conditions saccharin and sodium cyclohexylsulphamate were apparently harmless. Thus of the four sweetening agents that have been or are in use, two (dulcin and P 4,000) are clearly too toxic for human ingestion.

Colouring Matter

By far the most commonly used chemical substances for colouring belong to the azo-dye group. In the U.S.A. and Canada those azo dyes which can be used as food colourers are specified, but in this country only those dyes are named which may not be used. (In 1947 five of the coal-tar colours were officially included in this group, but the number may have increased since then.) In recent years, and especially since the great activity which followed the discovery of the carcinogenic action of polycyclic aromatic hydrocarbons and simple derivatives of these substances, the azo dyes have come under suspicion as being potentially toxic agents. These latter observations had their origin as long ago as 1906, when Fischer described the cell proliferation produced by the azo dye scarlet red, an observation later developed when this substance was used to accelerate the healing of wounds.

However, in 1932 Yoshida found that the addition of a related azo dye (*o*-amino-toluene) to the diet of rats produced malignant tumours of the liver. Even more potent as a liver carcinogen was another azo dye, *p*-dimethylamino-azobenzene, which had long been used as a food-colouring agent under the name of butter yellow. Cook *et al.* (1940) examined a large number of azo dyes for their carcinogenic properties and found a few to have this undesirable action. Kirby and Peacock (1949) showed oil orange E to be carcinogenic. The following azo dyes have been shown to have carcinogenic action, in most cases producing hepatomas when fed to rats: *o*-amino-azobenzene, *p*-dimethylamino-azobenzene (butter yellow), *p*-monomethylamino-azobenzene, *p*-amino-azobenzene, 2:2′-azonaphthalene, 1:1′-azonaphthalene, and benzene-azo naphthol (oil orange E).

Although the use of azo dyes in food preparation, especially those proved to have carcinogenic action, sounds unpleasant, there is probably no great cause for alarm. Primary hepatic carcinoma, which some of these dyes have been shown to produce in rats, is a rare condition in this country. In some tropical and subtropical countries, however, this morbid condition is common, although the amount of azo dyes consumed is probably *nil* or negligible. There is indeed evidence that in these latter countries hepatomas are the result of malnutrition, and seem to be associated in some way with a low-protein diet deficient in riboflavin. Thus the incidence of primary liver carcinoma throughout the world gives no support to the view that azo dyes in the food can be incriminated as a direct cause of the disease in man. While this is true, the only practical method of dealing with the problem is surely to exclude from human diet the dyes which are known to have such effects on animals, and it would also be advisable to have other dyes tested on animals *before* they come into use and not after their adoption.

Chemical Substances used in the Preparation of Bread and Cakes

These foodstuffs are so largely eaten that they demand particular attention, especially as they are probably more treated by chemicals than any other articles of dietary. Many of the chemical agents used seem to make the end-product more palatable to the average man or confer some benefit on the food. Some of these benefits, such as anti-staling and anti-rancidity, are of real value, while others only increase the aesthetic qualities of the product to the consumer.

Bleachers and Improvers

The following substances are used as bleachers and/or improvers: Nitrogen trichloride (NCl_3), chlorine dioxide (ClO_2), nitrosyl chloride (NOCl), nitrogen peroxide (NO_2), chlorine (Cl_2), potassium persulphate, ammonium persulphate, potassium bromate, benzoyl peroxide ($(C_6H_5CO)_2O$, calcium acid phosphate, calcium sulphate, ascorbic acid, succinic acid. Some of these substances (for example, NCl_3 and ClO_2) are both bleachers and improvers, some are only bleachers (NO_2, benzoyl peroxide), and some are only improvers (ascorbic acid, ammonium persulphate, potassium bromate).

The use of bleachers is claimed to be directly due to the preference of consumers for white rather than coloured bread. The same reason is offered for the preference for bread made from flour of low extraction,

as in this case the coloured portions of the grain—namely, the germ, aleurone layer, and bran—are eliminated. Although there may be some doubt about the direct and indirect harm bleaching does to the nutritive value of flour, there is no doubt that the removal of the germ and aleurone layer definitely lowers the value. As regards bleaching, the only observation I can make is that in my experience some bleached flour has a smaller amount of vitamin-A precursor, probably carotene, than unbleached flour. The amount of vitamin-A precursor in flour is very small in any case, and for people on a mixed diet its loss is probably of little significance. As for white flour of low extraction, it must be stated that, apart from any aesthetic attraction to the consumer, the miller has strong economic reasons for advocating it, for the wheat offal has a high value as an animal feeding-stuff.

From the point of view of the State the question of bleached flour reduces itself to the practical one, Would the non-fulfilment of the preference of the average man for white bread by supplying him with a nutritionally better but slightly coloured loaf be harmful? Surely the answer to the question was supplied during the war, when bread, even though it was made of flour of 85% or higher extraction, and was distinctly coloured, was eaten with pleasure by the vast majority of a remarkably healthy population.

The question of the use of flour improvers is also difficult. These substances make the loaf lighter by allowing more air and gas to be incorporated in it. Thus loaves of unit volume made from improved flour will contain less flour and more air and water than loaves made from untreated flour of similar size. It is said that the loaf volume is increased by improvers by 15–20%. Here again many people prefer these lighter loaves, as they are more easily masticated and pleasant to the mouth. If people prefer to eat bread which contains less sustenance and nutritional value per unit volume, it is difficult to see what can be done about it apart from official action. Both the producer and consumer seem satisfied—the one because he can make more loaves out of a given quantity of flour, and the other because he is prepared to buy bread of less nutritional value which he likes. The lower nutritional value of the improved loaf will alone cause the consumer to buy more bread to satisfy his needs. I shall return to this point later.

Toxic Effects of Agenization

How about the possible toxic effects of such chemical additions to flour? Although several official inquiries on this subject have been made in past years, it has only recently become one of great public interest, since the discovery that agenized flour (treated with NCl_3) causes hysteria or running fits in dogs. In the U.S.A. this discovery has led to an official decision on the part of the Government to exclude the use of agene as an improver—a decision which was quickly acted upon. Although a similar decision was made in this country some years ago, it has not yet been implemented, but no doubt in the future the agene process will also disappear from the United Kingdom, and it may be replaced by some other method of improving flour. In the U.S.A. nitrogen trichloride as a flour improver has been replaced by chlorine dioxide. Many tests have been made with ClO_2-treated flour, and up to the present no harmful effects have been observed in animals. No decision seems to have been made in this country regarding the improver to be used as a substitute for the agene process.

Those who favour the retention of the agene process or think that there is no need to hurry its ban from the milling industry point to the absence of evidence that agene-treated flour has a toxic action on man. It is quite certain that different species of animals differ greatly in their susceptibility to agenized flour, but it is equally true that no species of animal yet tested with the active principle—methionine sulphoximine—has failed to show severe toxic symptoms of the central nervous system when these tests have been systematically made; and it would be remarkable if man were an exception, especially if the dosage were raised. Monkeys are said to have about 100 times the resistance of dogs to methionine sulphoximine, and it is possible that man has a similar resistance as regards acute reaction to this substance. Nothing is known of the chronic toxic effects of agenized flour, and it may well be a matter of some importance to individuals who have been living on bread made from agenized flour over periods up to 25 years.

We certainly have enough chronic degenerative diseases of the nervous system of unknown aetiology to suggest that this matter is worthy of consideration. The present apparent official complacency to the ingestion of agenized flour in this country is disturbing, not only in itself, but because it indicates a reluctance to consider seriously the wider problem of chemical manipulation of food and its relation to health and disease. As agenized flour was widely consumed for nearly 30 years before its toxic action was discovered, it is very difficult to exonerate other improvers, even if in their case no harmful effect has yet been discovered. As stated previously, it is the unexpected that so often happens in matters of this kind.

Apart from the question of direct toxic action of the chemical improvers and bleachers added to flour or of any toxic agent they may produce in their reaction with the constituents of the flour, there is an aspect of the subject which does not seem to have been investigated. I refer to the possibility of the production of substances in these reactions whereby the availability or physiological use of essential factors in bread is modified. On the agenized flour analogy, where the NCl_3 clearly destroys some or much of the methionine of the gluten in the development of the toxic methionine sulphoximine, it would not be surprising if, for instance, it were found that others of these improvers and bleachers destroyed or modified one or more of the essential amino-acids of flour protein so that they became physiologically unavailable.

It may be added that one of the difficulties in dealing with this subject is that both millers and bakers use improvers—the millers generally under controlled conditions, the bakers sometimes in a more haphazard and indiscriminate way to produce a particularly desired property in the loaf according to the kind of flour at their disposal. The end-result is that by the time the loaf reaches the consumer its earlier chemical treatment and the results thereof must often be a matter of conjecture.

Probably enough has been said about improvers and bleachers of flour to suggest that the chemical manipulation of flour still requires further investigation, and that this practice should not be accepted uncritically as a safe and desirable food-processing treatment.

Replacement of Natural Fats in Food by Chemical Emulsifiers

One of the most remarkable groups of chemical substances introduced into food processing is that of "surface active" agents or emulsifiers. These fall into four classes: (1) mono- and di-glycerides of natural fatty acids; (2) a class of compounds produced by the reaction of sorbitol (a sugar alcohol) with a fatty acid; (3) compounds formed by the reaction of a sorbitan ester of a fatty acid with polymerized ethylene oxide; and (4) polyoxyethylene monostearate (by varying the fatty acid or the length of the polymerized ethylene oxide chain many compounds can be formed).

It was found in 1937 that by the use of the mono- and di-glycerides bread, buns, cake, and other sweet goods became more "tender." In 1947 the polyoxyethylene monostearate type of compound began to compete with the mono- and di-glycerides as bread softeners. In addition to their shortening and anti-staling effects, these substances are used as emulsifiers in preparing cake mixes and ice-cream, and also as dispersing agents in flavours, essential oils, and polyvitamin preparations.

As regards possible toxic action, no evidence of any such effect has been ascribed to mono- and di-glycerides even when ingested in large quantities. In the case of polyoxyethylene compounds there has been much controversy about their safe use in foods. This will be referred to only briefly, as the experimental evidence seems so conflicting. Polyoxyethylene glycols of molecular weight 1,250–3,600 have been used both in foods and in cosmetics. No ill effects were produced in rats when large quantities (20 g. per kg. per day) were included in the diet over a period of three months (Smyth *et al.*, 1942). Dogs were found to excrete the substance unchanged, so that it is evident that they do not depolymerize the compound into the poisonous ethylene glycol (Shaffer, Critchfield, and Carpenter, 1948). The same facts were shown to hold also for rabbits and man (Shaffer, Critchfield, and Nair, 1950).

The danger in such cases is the presence of the polymers of ethylene glycol in the less pure preparations. Here in fact is one of the many instances in food and drug work which show how essential it is to use chemicals of the highest purity; otherwise the effects may be disastrous. Medical men will need no reminder of the many deaths which resulted from the brief life of elixir of sulphanilamide when diethylene glycol was used as the solvent. This is a lesson which needs emphasizing in the case of all food adulterants.

Polyoxyethylene sorbitan monolaurate has been given to rats as 0.5–2% of their diet during their lifetime without obvious toxic effect, and 1 g. daily has been given to four monkeys without producing toxic effects (Krantz *et al.*, 1948). When the monostearate was incorporated at levels of up to 25% in the food of young rats, nasal haemorrhage, gangrene of the tail and legs, severe diarrhoea, and vesical calculi developed. At the level of 12.5% the rats were unaffected (Harris, Sherman, and Jetter, 1950). Evidence, however, has been more recently forthcoming to show that polyoxyethylene monostearate fed to hamsters at a level of only 5% of the diet was harmful in that some of the animals died, and in the surviving animals the growth was less than in the control animals given lard (Schweigert, McBride, and Carlson, 1950). Erosion of the mucous membrane of the intestinal wall was one of the pathological lesions produced (Wang, McBride, and Schweigert, 1950).

Coppock (1950), reviewing the evidence of the recent U.S.A. Bread Hearings, states that many of the polyoxyethylene compounds, including polyoxyethylene sorbitan mono-oleate and polyoxyethylene stearate, do not give rise to any obvious acute symptoms after oral administration, but that there is some evidence, both from animal experiments and from human studies, that gastro-intestinal disturbances occur. On the basis of the available evidence the Committee on Food and Nutrition of the U.S.A. has recommended that, until a uniform material is produced which conforms to a specification known to relate to a non-toxic product, these substances should not be used in the making of such a staple dietary product as bread.

According to the *Federal Register*, August 8, 1950, the U.S.A. Food and Drug Administration has proposed that lecithin and the mono- and di-glycerides of fat-forming fatty acids alone shall be permitted in the shortening used in American bread. The amount of the glycerides is restricted to a maximum of 25% by weight in the fat. No other surface-active compounds are recommended. Polyoxyethylene stearate, sorbitan esters of fatty acids, polyoxyethylene sorbitan esters of fatty acids, and the glycerides of acetylated tartaric acid are specifically excluded. Again we must await the official British reaction to the U.S.A. decision.

Reduction of the Nutritive Value of Food by Chemicals

Some of the actual and potential toxic actions of chemicals used in food preparation having been briefly discussed, let us now turn to the second problem—namely, the reduction of food value by these substances. There are instances in which chemical adulterants interfere with the absorption of essential factors of the diet, but this is not the type of case to be discussed now. The point to be considered is the situation caused by discoveries that some chemical agents of no use nutritionally to the body can confer on food preparations pleasant and acceptable gustatory properties which have previously been given to food by natural ingredients. The substitution of saccharin and other chemicals for sugar has already been mentioned.

Up to 1945 mineral oil was widely used throughout the country as a substitute for fat. For many years it had been used as a substitute for olive oil and other natural vegetable fats in salad dressing. During the war it became a popular ingredient of cakes as a fat substitute, and undoubtedly improved their texture and made them more acceptable than otherwise would have been the case. Mineral oil is for the most part passed through the alimentary canal unchanged and is a popular laxative. Its use in the U.S.A. was forbidden as a food adulterant not because it had no food value or because it was a laxative, but because it interfered with the absorption of vitamin A and caused in some infants a lipoid pneumonia. No doubt similar reasons formed the basis of its official rejection here. At the present time the use of mineral oil is confined to the greasing of baking-tins so as to prevent sticking.

But the introduction of polyoxyethylene derivatives and other substances as fat-sparers has raised this aspect of food treatment to a major issue. The Director of the Fats and Oils Branch of the Production and Marketing Administration of the United States Department of

Agriculture recently testified that the pre-war average use of fat per pound (454 g.) of flour in the baking industry was about 4% for bread and rolls; and that after the war and the introduction of emulsifiers the evidence indicated that the proportion was reduced to 1.5 to 2%. With the 2% figure this would amount to a reduction in the use of fat by the baking industry in the U.S.A. of about 160,000,000 lb. (72,575,000 kg.) annually. The proportionate reduction in fats used in baking by these fat sparers is probably not so large in this country, because bakers do not usually use the high amount of fat in bread-making as in the U.S.A., but still the principle is the same.

In addition these surface-active emulsifiers have the same property of increasing the size of the loaf as the improvers mentioned above. Thus Coppock found that, whereas the average volume of a loaf made without the addition of substances of the glyceryl monostearate type was about 1,358 c.cm., when these substances were added to the extent of 0.3% of the same flour weight the volume of the loaf increased to about 1,480 c.cm.—a reduction of 9% in the nutritive value per unit volume of the loaf. Coppock also found that by the use of polyoxyethylene stearate (0.5% of the flour weight) the average volume of the loaf was increased from 1,364 c.cm. to 1,651 c.cm. —that is, a reduction in the nutritive value per unit volume of loaf by about 20%. It is clear, therefore, that, quite apart from any question of toxicity, these anti-staling and crumb-softening agents have two actions which can be used to reduce the nutritive value of the loaf or other baking products. In the first place, as anti-staling and shortening agents they can replace fats, and, secondly, by increasing the volume of the loaf they reduce the food value per unit volume by a significant amount.

Summing up all these effects of flour treatment on the ultimate constitution of the loaf, we see that improvers used by millers might be expected to reduce the total energy value per unit volume of loaf by about 15 to 20%, and the baker's use of anti-staling agents by 9% up to 20%. In addition there is the possibility, just discussed, of substituting for fat in many foods the new emulsifiers. To this might be added the 10% reduction in protein value of flour by the proposed lowering of the extraction rate from 85% to 72%, together with the loss of mineral elements and of vitamins and probably many other unknown essential food factors. Many of these effects are additive and will undoubtedly result in products which are lighter, whiter, and more easily masticated, but of considerably reduced food value.

A worker in this field recently suggested that the ultimate goal of this general trend would probably be reached when a bread substitute made up primarily of starch, air, water, polyoxyethylene stearate, and a little saccharin was found acceptable to the general consumer. This exaggerated statement at least suggests the magnitude and importance of the present problem, and the time has come when the question of depressing the nutritional value of food as against the benefits brought by the use of chemical agents, even harmless chemical agents, will have to be decided.

Pesticides and Food Crops

Although there is general agreement that most food crops require the use of pesticides, the recent introduction into agriculture of some very toxic and effective substances of this class has raised much misgiving among health authorities. These include D.D.T., the first of the chlorinated hydrocarbon insecticides; chlordane, another insecticide of the same class which is four to five times as toxic as D.D.T.; and selenium compounds. Phenyl mercury compounds are used as fungicides on fruit and vegetable crops. It has been pointed out that as little as 2½ parts of chlordane per million in the diet produces pathological changes in the liver in rats, that 3 parts of the selenium compounds per million in the diet will produce cirrhosis of the liver and, if continued, cancer of the liver in animals; and that in the case of phenyl mercury compounds as little as 0.5 part of mercury per million in the liver in the form of phenyl mercuric acetate leads to measurable storage in the kidney with damage to that organ in animals.

The great drawback to the use of D.D.T. is that it is absorbed and stored by the body in the fatty tissues, and above a certain point of accumulation it injures the animal. Five parts in a million in the diet of rats produces definite liver injury (Laug, Nelson, Fitzhugh, and Kunze, 1950). Cows sprayed with D.D.T. or given silage which has been sprayed with it, or even housed in a barn in which it was sprayed, accumulate D.D.T. in their fat and eventually excrete it in the milk. The recent report from the U.S.A. that considerable quantities of D.D.T. have been found in the fat removed at operation from ordinary citizens is disturbing (Laug, Prickett, and Kunze, 1950).

But none of the above-mentioned chemical agents used as insecticides and fungicides have the intense toxicity of the organic phosphorus insecticides, the discovery of which as poison gases by the Germans led afterwards to their introduction to agriculture as insecticides and present extensive use throughout the world. Pharmacologically they are of great interest because they have an anti-cholinesterase action. While much is known about the acute toxic symptoms they produce, we have no information about the chronic effects. They are very useful in the control of a wide variety of pests such as aphides and red spider, and are of particular value against insects which may be resistant to D.D.T. and the older insecticides. As the action of many of these new insecticides depends on their absorption by the growing plants, the question of the effect on the consumer of eating such plants and their products, together with their spray residues, is clearly one of great importance. Sometimes the residues remaining on fruit and vegetables after spraying are high, and become particularly dangerous when they penetrate their skin. Thus it is said that selenium compounds accumulate in the apple in amounts up to 3 parts per million, a concentration which is known to be dangerous.

This subject is too big to discuss further here, but it may be stated that the official world that considers these matters must be cognizant of the dangers, because many people engaged in the preparation and use of these substances as insecticides have already been killed or injured by them (Bidstrup, 1950). The question is, What happens to the consumer?

Conclusion

Although it has been possible to consider only a few instances of the use of chemicals in food preparation and production, enough may have been said to show the vastness and importance of a problem closely bearing on the public health. The triumph of medical science in the prevention and control of disease during the present century has been impressive, and care must be

taken that, at the time of gaining such control, new habits of living which cause ill-health should either be prevented or, if they arise, be controlled. Such errors in living are undoubtedly developing at the present time, and it is the duty of medical science to find out their relative disease-producing importance. The chemical manipulation of food may well be the basis of some of these errors, and the problem requires investigation.

Official inquiry—both laboratory and judicial—and control want strengthening. There ought to be a practical counterpart in this country of the Food and Drug Administration of the U.S.A., in the form of either a public institute for such work or an extensive and close liaison with other institutions capable of making the necessary investigations. Official direction and control of and responsibility for all such matters should ultimately be placed with the Ministry of Health, as this is fundamentally a medical problem. Apart from chemicals long in use, a decision ought to be made on whether any new chemicals should be allowed in food processing and production before they have been adequately tested for their toxicological effects. No use of chemicals based on effective aesthetic or even practical advantages conferred on food by these substances should be countenanced if they have harmful effects on animals; and, apart from questions of toxicity, the present trend of lowering the nutritive value of extensively eaten food such as bread, both by chemicals and by other forms of manipulation, demands attention.

One final suggestion is that if people want bread which has not been chemically treated in any way they ought to be able to purchase it. This is no doubt possible in the case of wholemeal bread, but the same ought to apply to bread made of flour of lower extraction. At least untreated flour of this kind ought to be freely available so that persons can bake their own bread if they wish.

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ACUTE TUBERCULOUS SEPTICAEMIA WITH LEUCOPENIA

BY

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Acute tuberculous septicaemia presents as an obscure clinical picture, with pyrexia, severe leucopenia, and a rapid downhill course. No case so far recorded has been diagnosed during life, but in view of the possibility of chemotherapy an early diagnosis is very desirable. Three cases will be described. They were observed on the same medical unit within four years, which alone suggests that this form of tuberculosis is commoner than is usually believed.

Case 1

A plasterer aged 54 was admitted on April 17, 1946. He had been well until three weeks previously, when he developed rigors followed by severe sweating. The personal and family histories were not significant. On examination he was very ill. He had herpes labialis, a furred tongue, and petechiae on the chest. There was an impaired note with diminished breath sounds at the right base. No abnormal signs were present in other systems.

White cells numbered 925 per c.mm. (neutrophils 72%, lymphocytes 21%, monocytes 5%, eosinophils 2%). The white cells rose later to 1,100 and 1,450, with 86% neutrophils on each occasion. Haemoglobin, 89%; red cells, 4,400,000; colour index (C.I.), 1.0. Sputum gave a growth of *Staph. aureus* and pneumococci. No tubercle bacilli were seen. *X*-ray films of chest showed some consolidation at both bases.

His temperature was irregular up to 101° F. (38.3° C.). A diagnosis of pneumonia with leucopenia was made, and he was treated with penicillin and liver extract. He steadily became worse and died on April 24.

Summary of Necropsy and Histological Findings

(For anatomical details, see Blair and Pagel, 1947.) The main feature was the presence of extensive naked-eye changes in the spleen, liver, and mesenteric lymph nodes. There were areas of necrosis full of acid-fast bacilli and devoid of the classical tuberculous cells. The shadowy preservation of the organ structure in the necrotic areas suggested that it was an example of "direct necrosis." (For definition, see Case 3.)

Careful dissection and post-mortem radiography failed to detect any traces of old or fresh tuberculous changes in the lung. Extensive fresh caseation of the mesenteric lymph nodes, however, suggested that the intestinal tract was the portal of entry.

The numerous areas of necrosis full of tubercle bacilli which were present in the marrow of the sternum and the femur were regarded as the cause of the leucopenia.

There was haemorrhagic consolidation of the basal part of both lower lobes. The alveolar exudate was full of cocci, but no acid-fast elements were seen.

Tubercle bacilli of human type were recovered from a mesenteric lymph node.

Case 2

An insurance agent aged 56 was admitted on May 5, 1947. He had been well until one month previously, when he had fainted in the street and bruised himself. He later developed a rash on his face, arms, and legs, and twitching of the face.

On examination he was seriously ill. His tongue was heavily coated and his throat was red, although no exudate was seen. Sonorous rhonchi were present over both lungs. He had a regular tachycardia of 168, which was found to be due to a 2:1 auricular flutter. No abnormal signs were found in the central nervous system or the alimentary system.

White cells numbered 2,050 per c.mm. (neutrophils 46%, lymphocytes 48%, other cells 6%). Haemoglobin, 78%; red cells, 3,100,000; C.I., 1.25. The white cells later fell to 500 and 250, the majority being lymphocytes. An *x*-ray film of the chest showed patchy consolidation of the right lower lobe. The cells in the cerebrospinal fluid were normal, but the protein was 55 mg. per 100 ml.

A diagnosis of bronchopneumonia with leucopenia was made. There was an intermittent pyrexia up to 101° F. (38.3° C.), and he was treated with penicillin, pyridoxin, and folic acid. Despite full dosage of digitalis the auricular flutter persisted, and he died on May 18, five weeks after the onset of his illness.

Summary of Necropsy and Histological Findings

(For anatomical details see Pagel and Woolf, 1949.) A fresh caseous primary complex was found in the right lower lobe of the lung, consisting of a large wedge-shaped caseous area and enlarged caseous bifurcation lymph nodes.

There was haemorrhagic consolidation of the lower lobes near the base, with many cocci but no acid-fast elements visible in the exudate.

The spleen showed no naked-eye changes other than an anaemic infarct near the upper pole. Histologically, this was due to endophlebitis with innumerable acid-fast bacilli in the swollen and fibrinoid-necrotic intima.

A small anaemic infarct in one kidney was due to an arterial thrombosis, without evidence of a tuberculous origin.

There was no naked-eye evidence of multiple necrotic foci as seen in Case 1, but, histologically, innumerable ill-defined small areas of necrosis, teeming with acid-fast bacilli, were seen in the spleen, liver, suprarenals, and bone marrow (femur and sternum).

Tubercle bacilli of the human type were recovered from a bifurcation lymph node and from the spleen.

Case 3

A housewife aged 47. Apart from an attack of "congestion of the lungs" in 1946, she had been well until three weeks before admission on July 19, 1949. Since then she had been feverish, with anorexia and malaise, and had become much worse on the day of admission. On account of her confused state she was admitted to the mental observation ward.

On examination she was severely toxic, with a temperature of 103° F. (39.4° C.) and a pulse of 128. Her tongue was dry and furred, and there were a few petechiae on her back and abdomen. There were no abnormal signs in the lungs, but her spleen was easily palpable. The general picture strongly suggested typhoid fever.

The white cells totalled 700 per c.mm. (neutrophils 70%, lymphocytes 30%). The count rose to 1,900, but later fell to 400. The proportion of neutrophils was never less than 48%. Haemoglobin, 58%; red cells, 3,200,000; C.I., 0.9; platelets, 30,000. Cerebrospinal fluid was normal. Agglutinations against *Salmonella typhi* and *paratyphi* were negative. Sternal puncture showed reduction in cellularity due to a marked diminution of the granulocytes and their precursors; the van den Bergh test gave a positive delayed direct reaction, with bilirubin 2 units. Serum proteins: albumin 1.8, globulin 3.7 g. per 100 ml.

Typhoid fever was soon excluded, but the cause of the leucopenia remained obscure. It was thought that she might have been taking some drug, but no evidence of this could be found. Primary agranulocytosis and miliary tuberculosis were also considered. She was treated with penicillin, liver extract, and bone-marrow extract, but steadily deteriorated, became jaundiced, developed ulceration of the fauces, and died eight days after admission.

Necropsy: Summary of Naked-eye Changes

Multiple subpleural petechiae, with basal haemorrhagic consolidation, were present in both lungs. A small subpleural necrotic nodule was found in the left lower lobe, associated with extensive greyish-white necrosis of the enlarged bifurcation and left lower bronchopulmonary lymph nodes. In the mesentery, near the ileocaecal junction, there was a hard calcified lymph node. The liver was jaundiced and enlarged, and showed no focal changes. The spleen weighed 280 g. and also showed no focal changes. The kidneys were normal in size and appearance. The femoral marrow was dark red.

Histological Examination

The left bifurcation lymph node was almost completely replaced by confluent oedematous areas of necrosis containing round chromatin fragments but with no cellular response at the periphery. Round chromatin debris is due to a process of "direct necrosis" of the lymphocytes without previous "tuberculization," and should be distinguished from "caseation," which follows the conversion of the tissue cells into epithelioid and giant cells. Since the nuclei of these cells are spindly or varying in shape, so are their chromatin fragments. Many colonies of long granular acid-fast bacilli were found in the necrotic areas (Fig. 1).

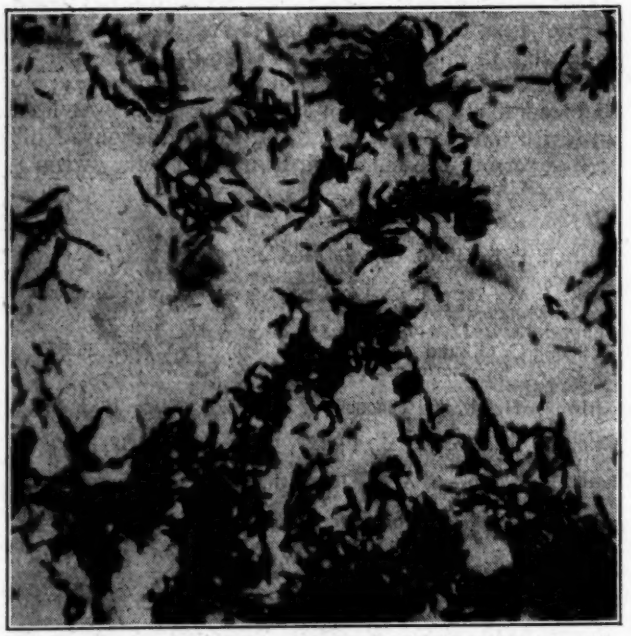

FIG. 1.—Case 3. Hilar lymph node, showing long beaded acid-fast bacilli. (×900.)

The basal parts of the lung showed a confluent pneumonia. The focus described in the left lower lobe consisted of a number of small ill-defined necrotic foci with a tendency to confluence, some of which seemed to have developed in the intima of a pulmonary vein. In the spleen the Malpighian corpuscles were scanty and were mostly replaced by collections of plasma cells and mononuclear cells. The pulp was very cellular, with many swollen reticulum cells and histiocytes. Some of the large mononuclear cells contained long granular acid-fast bacilli. In the liver small focal collections of swollen histiocytes containing acid-fast bacilli were seen in many sinusoids. The fat marrow had numerous "active" islets, in which large reticulo-endothelial

cells containing acid-fast bacilli predominated. There were also small areas of necrosis containing bacilli (Fig. 2). The adrenals showed no evidence of necrosis. An abdominal lymph node showed a typical calcified primary focus with marginal ossification. There was no evidence of recrudescence.

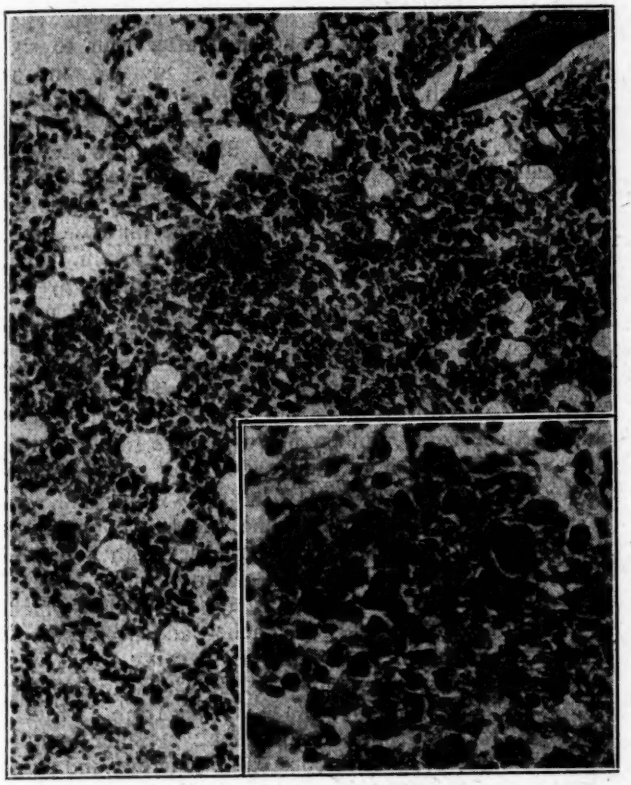

FIG. 2.—Case 3. Bone marrow (sternum), showing ill-defined areas of necrosis; ×100. Inset: Close-up of central focus; ×250.

Bacteriology

Cultures from the caseous bronchial lymph node were contaminated, but an inoculated guinea-pig developed an enlarged deep inguinal lymph node as the sole lesion. Cultures from the guinea-pig produced a profuse growth of an acid- and alcohol-fast bacterium which was not characteristic of either a human or a bovine tubercle bacillus. Inoculation into a guinea-pig produced a local granuloma only. It is therefore not certain that the organism cultivated was the cause of the disease.

Comments on Case 3

There are the unmistakable traces of healed *primary intestinal infection*. This must have occurred years ago, as the calcified abdominal lymph node is partly ossified.

The present condition is unrelated to primary infection. It presents the features of *genuine reinfection*. By this we understand a renewed infection from without. It causes a caseous focus, to be found at the portal of entry, followed by a caseous change (or, as in the present case, "direct necrosis") in the regional lymph nodes—in other words, a new lesion of the primary complex type. It is supposed to occur when allergy has disappeared as the result of a complete healing of the primary complex. In the present case, gross involvement of the hilar lymph nodes by a widespread and rapid process of direct necrosis was impressive.

There is evidence of extension into a pulmonary vein, although it could not be proved that this was due to direct communication of the vessel with a lymph node which had ruptured into it.

Generalized spread, notably to the liver, spleen, and bone marrow, followed. The changes found in these organs present a slightly different picture from that seen in most cases described. First of all, there were no naked-eye changes. Secondly, necrotic foci were missing in the sections of the liver, were scarce in those of the spleen, and were small in extent in the bone marrow. Apart from "direct necrosis" of unchanged tissue elements a cellular reaction preceding necrosis is indicated by the small collections of reticulo-endothelial cells, as seen in the liver and spleen. These showed beginning nuclear degeneration and were full of acid-fast bacilli.

Small areas of necrosis were most widespread in the bone marrow, and explain the blood changes.

The pathological changes described must be attributed to the action of acid-fast bacilli which were present in all of them; and, vice versa, wherever acid-fast organisms were seen they were associated with such changes. Thus it can be concluded from the histological picture that these organisms were not secondary invaders.

Discussion

Definition and Frequency

"Acute tuberculous septicaemia" is a rare condition. Altogether about 30 cases can be collected from the literature (von Wyss, 1940; Blair and Pagel, 1947; Pagel and Woolf, 1949). A number of these cases are based on very scanty post-mortem data, and should be ignored, as should those that have been described from clinical evidence alone (so-called "typhobacillosis").

A further reduction will depend upon the strictness of definition. "Acute tuberculous septicaemia" in the strict sense means an independent manifestation of tuberculosis. It is marked by a spread of necrotic foci without the usual tuberculous features other than the presence of acid-fast bacilli. This definition excludes:

(*a*) Cases mixed with or following on miliary or other clinical tuberculosis.

(*b*) Those without histological data.

(*c*) A considerable number of observations representing the terminal states of a blood disease (for example, myeloid leukaemia, pernicious anaemia, Hodgkin's disease, polycythaemia). There were no fewer than 7 such cases out of 18 collected by von Wyss from the literature. In addition, four out of the eight cases collected from necropsy material at Zurich by the same author belonged to this category. Two of the remaining four cases showed a severe leucopenia, and these are included, since, unlike the other blood diseases mentioned, the blood condition appears to be a result rather than a cause of tuberculous septicaemia.

Pathogenesis

Acute tuberculous septicaemia follows fresh primary infection or, as in Case 3 of the present series, reinfection. The portal of entry is not infrequently the gastro-intestinal system (9 out of 15 cases with relevant data). This need not necessarily mean bovine infection; for human strains have been recovered in spite of intestinal infection (Jacobowitz, 1934; Siegmund, 1939; Blair and Pagel, 1947). The peculiar character and course of the disease do not therefore seem to be explained by any special characteristics of the bacterial strains involved.

We are ignorant of the causes which enable the tubercle bacillus to set up an overwhelming generalized infection without cellular response. It may be that an age factor is operative, the majority of the cases involving

higher age groups. A special condition of the haemopoietic system may be derived from the occurrence of an acute spread similar to fulminant tuberculous septicaemia in the terminal phases of blood diseases. It should be emphasized, however, that we have no evidence of a primary failure of the body to produce cells, notably polymorphs, to account for the peculiar lack in resistance. Tuberculous septicaemia is observed in leukaemias with superabundant circulating cells, and usually fails to appear in ordinary agranulocytosis. In some cases leucopenia can be shown to set in after the acute illness has developed. Finally, there are no data in the general and experimental pathology of tuberculosis which would support the hypothesis of diminished antituberculous resistance due to a primary damage to the leucocyte-forming systems (Pagel, 1948).

Anatomical Forms

According to post-mortem findings, two categories can be distinguished : (*a*) cases with naked-eye changes —to wit, a spread of necrotic foci usually twice or three times the size of miliary nodules (these are found in the spleen and liver) ; (*b*) those without characteristic naked-eye changes. There may be the simple "septic changes," such as subserous petechiae, or a "septic spleen," or a few simple infarcts. The majority of cases belong to category (*a*) ; for example, all but one of the 30 cases reviewed by von Wyss (1940). Apart from the case of Scholz (1918), those reported by Pagel (1927), Pagel and Woolf (1949), and Case 3 of the present series fall under category (*b*). In other words, these cases seem to be particularly uncommon.

Clinical Features

Only eight other fully recorded cases could be found in which severe leucopenia was associated with post-mortem evidence of acute tuberculous septicaemia, although there are several reports of cases with normal or unrecorded white counts (von Wyss).

Scholz (1918) reported the case of a woman of 56 who died after four weeks' febrile illness. She was jaundiced and her spleen was palpable. The leucocyte count varied from 1,650 to 1,800 per c.mm., with a neutrophil percentage of 11–23. At necropsy, enlarged bronchial lymph nodes, a necrotic laryngitis, and a soft enlarged spleen were found. The liver and spleen contained numerous small necrotic foci with abundant tubercle bacilli.

Nasse's (1931) patient, a man of 53, was ill for six weeks before death with fever, cough, and anorexia. Leucocyte counts of 1,333 and 1,777 per c.mm. were recorded without differential counts. Necrotic foci containing tubercle bacilli were found in the lungs, liver, and spleen at necropsy.

Steinbrinck (1938) recorded the case of a man who died after a febrile illness of two to four weeks. The spleen was palpable. The leucocyte count fell from 1,700 to 400 per c.mm. with 6–8% neutrophils. The haemoglobin was 38%. Sternal puncture showed marked diminution of the neutrophil series. Necropsy revealed small areas of necrosis in many organs, all of which contained tubercle bacilli.

Müller (1938) described the case of a man of 54 who died after six weeks' illness with fever, cough, and malaise. The spleen was palpable. Leucocytes numbered 500–1,000, with 51–75% neutrophils. Haemoglobin was 38–44%, and sternal puncture was normal. Necropsy revealed caseating mesenteric, retroperitoneal, and inguinal lymph nodes, with large irregular tuberculous lesions of the spleen. Tuberculous lesions of the kidney and liver were also present. The spleen had necrotic foci containing tubercle bacilli ; the liver contained tubercles with giant cells and central necrosis.

Von Wyss (1940) recorded two cases of his own. His Case 6 was a man of 35 who died after four to six weeks' illness, characterized by sweats, malaise, and a morbilliform rash. The liver and spleen were enlarged. Leucocytes numbered 370 to 670 per c.mm. with 45–56% neutrophils ; haemoglobin 51%. Blood culture grew a non-haemolytic streptococcus. Necropsy showed chronic tuberculosis of the left upper lobe and miliary necroses in the liver, spleen, lungs, kidneys, bone marrow, and lymph nodes containing human tubercle bacilli. His Case 7, a woman of 35, had been taking amidopyrine tablets for headaches for five years. She died after three weeks' illness in which she had a high fever, rigors, and vomiting. Apart from a papular rash on the legs, there were no special clinical findings. The leucocytes fell from 6,000 to 800 per c.mm., with 2.5–11% neutrophils. At necropsy, miliary necroses were found in the lungs, spleen, and bone marrow. The marrow also showed a marked diminution of granulocytes.

Siegmund (1939) reported nine cases of a reactive generalized tuberculosis. Of four cases with a severe leucopenia, only one was reported in detail. A man aged 29 died after three months' illness, during which he complained of tiredness, headaches, and sleeplessness. He ran an intermittent fever, but no cause for it was found. The leucocyte count fell from 3,000 to 425 per c.mm., the neutrophil percentage varying from 52 to 91. Necropsy revealed innumerable small necrotic foci in the lungs, spleen, lymph nodes, bone marrow, and skin. These foci contained tubercle bacilli, which were found to be of human type. An ulcer of the stomach was the site of a recent primary infection, which was associated with enlarged lymph nodes in the region of the pancreas.

Kernohan (1950) recorded the case of a man aged 61 who died 17 days after admission to hospital. He had been unwell for five months. Pyrexia, pallor, and enlargement of the liver and spleen were noticed. He had an aplastic anaemia (haemoglobin 36%) with 1,200 white cells. Sternal marrow examination revealed aplasia. The spleen showed multiple areas of necrosis with a slight mononuclear reaction around the margins. Acid-fast bacilli were found in the lesions. The picture was that of an atypical miliary tuberculosis.

Thus, including our three, 11 cases of acute tuberculous septicaemia with leucopenia have been fully recorded. The ages varied from 22 to 56, with an average of 44 years. Eight were men and three women. The acute illness, which was invariably fatal, lasted between three and twelve weeks. Rigors, anorexia, and malaise were the most frequent symptoms, and all cases ran a high fever of no constant type. The spleen was enlarged in six cases and the liver in three. Jaundice was present twice. In two cases there was a history of widespread skin eruption before admission, and a third case was found to have a papular eruption on the legs. Ulceration of the fauces was noticed only twice during life, just before death, although it was found in two other cases at necropsy. In 8 of the 11 cases the total leucocyte count fell below 1,000 per c.mm., but in only three of the nine cases in which differential counts were made did the neutrophil percentage fall below 40.

The haemoglobin was 60% or below in 6 out of 10 cases in which it was recorded, and the colour index was usually high. The platelets were recorded as being markedly diminished in three cases. Sternal puncture revealed a depression of the granulocytes in two cases, aplasia of the bone marrow in a third case, and a normal marrow in a fourth. Thus it appears that a depression of one or all of the blood-forming elements usually occurs.

Although severe leucopenia has been a striking feature of all the present cases, it is a complication rather than an essential feature of the disease, since it is, in our opinion, caused by the action of the tubercle bacillus on the bone marrow. In only one of the above cases (No. 6) was there evidence of a drug playing a part in the development of the leucopenia. In some of the cases the initial leucocyte count was normal or only slightly depressed, the severe leucopenia developing later. Nevertheless, its importance is stressed because it should prove one of the few helpful diagnostic features in a disease in which a correct diagnosis has apparently never been made during life.

Since the disease runs a rapid downhill course, an early diagnosis would have to be made if chemotherapy were to be given a chance of success. The most important factor in making the diagnosis would be to consider the possibility of acute tuberculous septicaemia in cases of high fever associated with leucopenia. The clinical picture often suggests typhoid fever or miliary tuberculosis. Splenic enlargement, abnormal chest signs, skin eruptions, and jaundice may also be present. A certain diagnosis could be made only by finding the tubercle bacillus. Since large numbers of tubercle bacilli can be found in the bone marrow post mortem, von Wyss has suggested that sternal puncture should be performed in an attempt to find the causal organism. Horowitz and Gorelick (1951) have described a method by which tubercle bacilli were demonstrated in the bone marrow in 14 out of 20 patients with advanced tuberculosis. This would seem to be the most likely way of confirming the diagnosis. Aspiration biopsy of the liver might also prove diagnostic.

It is possible that streptomycin might result in a cure if it were administered before irreversible changes had occurred. A trial of the drug would be fully justifiable in what is otherwise a hopeless condition.

Summary

Three cases of acute tuberculous septicaemia with leucopenia are described, and are compared with eight cases which have previously been recorded in the literature.

Rigors, anorexia, and malaise were common symptoms. A high fever was always present and an enlarged spleen was often felt.

A severe leucopenia without a striking relative neutropenia was the commonest finding in the blood. An aplastic anaemia and a thrombocytopenia were also seen.

A rapid downhill course invariably occurred, with death between three and twelve weeks from the first symptom.

Acute tuberculous septicaemia followed a fresh primary infection or a genuine reinfection in each of the three cases.

At necropsy, multiple necrotic foci were seen in the liver and spleen in Case 1, but in Cases 2 and 3 no characteristic naked-eye changes were visible in any organ.

In all cases histological examination revealed numerous necrotic foci containing acid-fast bacilli in many organs.

It is considered that the occurrence of these organisms in the bone marrow accounts for the leucopenia and anaemia.

The difficulty in diagnosis lies in the absence of characteristic features in this disease. Examination of the bone marrow for tubercle bacilli is recommended. Streptomycin should be given a trial in a suspected case.

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ACROSCLEROSIS

BY

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AND

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Scleroderma is a condition which may present in several ways. In its commonest form it appears as localized areas in the skin which show thickening, adhesion to the subcutaneous tissues, a smooth waxy surface, and progression to atrophy. This form—localized scleroderma or morphoea—is a disease of little consequence. The generalized form is a serious disease. The skin changes are similar, but large areas of the body are affected and the disease is steadily progressive. It is usually insidious in onset and runs a chronic course, but rarely may occur in acute form with rapid development of the typical changes. Among patients with generalized scleroderma it is possible to separate a group in whom the skin changes are confined to the hands, forearms, face, and upper chest, and are commonly preceded by Raynaud's phenomena in the hands. There is some dispute whether this form, which has been given the name of acrosclerosis, is a disease *sui generis* or is merely one way in which generalized progressive scleroderma may present.

Hutchinson (1893, 1895, 1896) seems to have been the first to recognize the association of Raynaud's phenomena with sclerodermatous changes. He separated such sclerodermatous changes from those of "diffuse scleriasis," not only because of their intimate association with Raynaud's phenomena but also because the skin changes were confined to the digits and, less often, to the face. He used the terms "acrosclerodermia," "acroteric morphoea," and "acroteric scleriasis" to cover the condition. Sellei (1931, 1934) likewise separated acrosclerosis from chronic progressive scleroderma and strongly supported the view that it is a disease in its own right. O'Leary and Waisman (1943), in an admirable account of the condition, also regarded it as

an entity. The main differences between acrosclerosis and generalized scleroderma are shown in the Table.

Main Differences Between Acrosclerosis and Generalized Progressive Scleroderma (Condensed from O'Leary and Waisman's Data)

	Acrosclerosis	Generalized Progressive Scleroderma
Sex	Mainly women	Men and women equally
Onset	In fingers, usually preceded by Raynaud's phenomena	Most commonly on trunk. Raynaud's phenomena rare and do not occur at onset
Distribution ..	Hands, forearms, face, and upper chest	Trunk, limbs, and face
Visceral lesions ..	Frequent (particularly oesophagus)	Rare
Prognosis ..	Favourable so far as life is concerned. Local changes may be arrested	Bad. Most of body involved after 2 years. Arrest rare

The frequency of visceral lesions in acrosclerosis is an important distinguishing feature and has been emphasized by Olsen, O'Leary, and Kirklin (1945). Among 350 patients seen at the Mayo Clinic with scleroderma or acrosclerosis, 36 had dysphagia or lesions of the oesophagus. Of these, no fewer than 33 had acrosclerosis. (Unfortunately the authors do not state how many of their total series were diagnosed as acrosclerosis, so the frequency of oesophageal lesions in this condition is not apparent.) Eighteen of these cases with positive radiological or oesophagoscopical evidence of oesophageal lesions are discussed in detail, and it is of interest that all these patients had Raynaud's phenomena preceding or coincident with the development of cutaneous lesions. In this country, Bourne (1947, 1948, 1949) has reported four cases of acrosclerosis with oesophageal lesions. Although the oesophagus is the most commonly involved of the viscera, lesions have also been recognized in other parts of the gastrointestinal tract, the heart, and the lungs (Weiss *et al.*, 1943; Bevans, 1945; East and Oram, 1947; Mathisen and Palmer, 1947; Dostrovsky, 1947). We present below the case reports of four patients with acrosclerosis who illustrate various aspects of the condition.

Case 1

This patient was an unmarried female clerical worker aged 29. At the age of 18 she developed "arthritis" of the hands and also of other joints. At 22 she had attacks of Raynaud's phenomena which have persisted until the present. At 23 the little finger was amputated because of trouble resulting from the local injection of some agent intended to dissolve restricting fibrous tissue attributed to the "arthritis." A right cervical sympathectomy was performed when she was 26; this was complicated by an arterial thrombosis in the right arm, and left her with Horner's syndrome in the right eye. The sympathectomy did not relieve her Raynaud's phenomena. At the age of 23 she developed mild indigestion; this grew steadily worse and became her most troublesome symptom by the time she was 27. It took the form of a retrosternal pain, which was exacerbated by swallowing food. She had for a considerable time also noticed some difficulty in opening the mouth fully. At this stage she was admitted to the Radcliffe Infirmary.

On examination her face was rounded and smooth, with a notable absence of normal furrows, so that she wore a doll-like expression. The skin had a waxy texture and was not easily moved over the forehead. The mouth was conspicuously small. The hands showed contractions of the fingers without any obvious deformity of bones or joints. The skin was smooth, shiny, thin, and fixed to the underlying tissues. Similar skin changes, though less severe, were present over the lower forearms and on the neck, where slight pigmentation was present in a reticular pattern. The right radial pulse was absent. Other systems were normal.

A barium swallow revealed very feeble peristalsis, stricture of the lower end of the oesophagus above the cardia, and a short oesophagus with a gastric pouch above the diaphragm; these appearances resemble a congenitally short oesophagus. Oesophagoscopy showed a stricture at the lower end of the oesophagus with oesophagitis and ulceration proximal to it.

It was found impossible to dilate the oesophageal stricture, mainly because the oesophagus bled freely with instrumentation. In consequence she was treated conservatively on the lines of a peptic ulcer of the oesophagus, but she failed to respond to this, both symptomatically and as seen at oesophagoscopy. Gastrostomy was performed in November, 1948, but she tolerated this poorly and continued to have restrosternal pain, so that in January, 1949, transthoracic partial oesophagectomy was carried out. Histological changes typical of scleroderma were found in the operation specimen. Persistent discharging sinuses followed the operation and she developed a severe anaemia, which required treatment by transfusion. Retrosternal pain continued and occult blood was still present in her stools. A barium swallow on March 29, 1950, showed a deformity suggestive of an ulcer crater at the junction of the oesophagus and stomach.

Comment.—This patient shows a typical distribution of skin changes, the usual early limitation of joint movement, the early occurrence of Raynaud's phenomena, and oesophageal involvement. She thus appears to be a classical example of acrosclerosis as described by O'Leary and Waisman (1943). It is questionable whether partial oesophagectomy was advisable. Olsen *et al.* (1945) recommended treatment by dilatation alone, but in this patient attempts at dilatation were unsuccessful. However, as it is difficult to excise all diseased tissue, it seems wise to resort to surgery only when all other methods of treatment have failed.

Case 2

A housewife aged 40 had suffered from attacks of Raynaud's phenomena from the age of 14. In cold weather her fingers would become white and numb. Her toes were slightly affected in the same way. At the age of 38 the picture changed: her fingers became swollen, blue, and mottled, and attacks of whiteness and numbness were superimposed. Her fingers were swollen and congested all the time, so that she could not hold things properly. She felt "run down" but had no specific complaints.

On examination her fingers were blue, mottled, and swollen, with limitation of movement. Other systems normal. The haemoglobin was 14.1 g. per 100 ml., and the E.S.R. was 23 mm. in one hour (Westergren).

Raynaud's disease was originally diagnosed. A sympathetic block with procaine hydrochloride caused the ipsilateral hand to become warm and flushed, and the skin temperature rose 10° C. Pre-ganglionic cervical sympathectomy was therefore carried out on the right and, later, on the left sides. After the operation her fingers still went blue in cold weather, but they were no longer painful. The stiffness steadily increased. She now had difficulty in moving her joints, not only those of the fingers but also her wrists, elbows, feet, knees, and hips. Later she noticed subcutaneous nodules in the region of the wrists, elbows, and knees, and that her tongue was becoming difficult to move. Her fingers showed typical sclerodermatous changes, and the skin of her face showed changes similar to, though less severe than, those of Case 1. The face changes were not recognized when she was first seen, and her whole history suggested that the condition was in a stage of progression. She has also developed patchy pigmentation of the arms and abdomen. Her joints were clinically normal, but there was marked tendon crepitus over the dorsum of the hands.

Dysphagia was not present, but a barium swallow showed involvement of the oesophagus.

Comment.—In this case Raynaud's phenomena preceded sclerodermatous lesions by many years. In this connexion it is interesting that O'Leary and Waisman (1943) and Olsen *et al.* (1945) often found this time relationship, and were led to believe that the sclerodermatous changes of acrosclerosis were a direct consequence of vasomotor disturbances. The favourable response to sympathetic blockage with procaine suggests that vasomotor changes were responsible for some of her symptoms (pain and coldness of the fingers), and that these were ameliorated by sympathectomy, whereas those which can be attributed to sclerodermatous changes have progressed since operation. The subcutaneous nodules in this case are similar to those found in many patients with rheumatoid arthritis. Radiological examination did not reveal any calcification.

Case 3

A housewife aged 61 developed indigestion at the age of 16 which has continued in periodic attacks ever since, the symptoms being like those of a peptic ulcer; over the past few years these symptoms have improved. There had never been dysphagia until recently, when she noticed that solid particles sometimes stick in her chest, causing choking fits. All her life she has suffered from chilblains. At the age of 31 pigmentation developed in the hands and arms, which progressed and involved the chest, neck, and abdomen. In 1943, at the age of 54, she developed swelling of the ankles, breathlessness on exertion, and attacks of Raynaud's phenomena of the hands. The attacks were precipitated by cold and were typical, but it was noticed that swelling of the fingers persisted during warm weather. Her feet have been slightly affected, chiefly in that they easily become cold. The oedema of the ankles subsides completely if she rests.

Since 1943 these symptoms have all become more severe, and in addition she has developed sores on her finger-tips and mild "arthritis" of shoulders, hips, and knees. She has lost weight and has not felt well. In 1948 a right cervical sympathectomy was attempted through an anterior approach, but had to be abandoned because of a large substernal goitre which impeded access; the brachial artery was stripped in place of sympathectomy, but with no effect on the symptoms. In 1949 left cervical sympathectomy was performed, also without effect. At various times she has been treated with thyroid extract, vitamin E, and vitamin K, but with no benefit. There was no clinical evidence of thyrotoxicosis and the B.M.R. was normal.

When seen by us in 1950 she exhibited the features of acrosclerosis in their most florid form. Her fingers were swollen, and the waxy inelastic skin could not be moved over the phalanges. The tips of the fingers showed necrotic areas, which were scabbed and scarred. Her fingers were stiff and incapable of full movement. The skin of the dorsum of the hands and the forearms was thickened and inelastic. There was patchy brown pigmentation of the whole body, with a few areas of vitiligo. The skin of the face was typically affected, being smooth and waxy with a notable absence of wrinkles and furrows except for deep creases converging on the mouth, which could not be opened widely (see illustration). It is interesting that in 1949, before the diagnosis was made, the case notes record that she "looks 20 years younger than her age." She also had numerous small red spots (telangiectases) over the upper part of her body. The abdomen and feet showed a few areas of morphoea. There was oedema of the ankles and feet. The chest moved well, and the lungs were clinically normal, apart from crepitations over both bases. The heart was enlarged clinically, but the heart sounds were normal and the rhythm was regular and slow. Her blood pressure was 125/75.

The blood W.R. and Kahn test were negative. The haemoglobin was 13.9 g.%; E.S.R., 17 mm. in one hour (Westergren). An E.C.G. showed normal rate and rhythm, negative T_2 and T_3, and R_3 varied from one ventricular complex to another, sometimes being well marked, at others non-existent.

A barium swallow did not reveal any hold-up to the passage of the barium cream; the oesophagus was tortuous, dilated, and showed very feeble irregular contractions. A radiograph of the left hand showed erosion of the tips of the terminal phalanges of the thumb and second, third, and fifth fingers, and calcified deposits in the soft tissue of the tip of the thumb. A radiograph of the right hand showed erosion of the tips of the terminal phalanges of the thumb, first, second, and third fingers, and calcified deposits in the tips of the thumb and first finger. *X*-ray examination of the chest revealed partial collapse of both bases, substernal thyroid with displacement of trachea to left, and old resection of the fourth left rib posteriorly. On screening, the cardiac pulsations were of conspicuously small amplitude.

Photograph of Case 3, showing typical facial appearance in acrosclerosis.

Comment.—This patient shows the coincidence of Raynaud's phenomena and well-marked changes of acrosclerosis. The distribution of skin changes is typical, but in addition she has a few areas of morphoea on the trunk. The oesophagus shows dilatation with diminished peristalsis, and it is therefore likely to be affected. It is probable that the heart is also involved, because the cardiac symptoms—breathlessness and oedema of ankles—accompanied the development of acrosclerosis; there is no other obvious cause for cardiac failure, and the poor movements of the heart observed on screening are compatible with this diagnosis. These details are similar to those shown by some patients described by Weiss *et al.* (1943) in whom the diagnosis was clinched at necropsy. Our patient also shows calcinosis of the finger-tips. This rare condition is not infrequently found in association with acrosclerosis (Sellei, 1931; Brody and Bellin, 1937) and the combination has earned the eponymous title of Thiblerge–Weissenbach syndrome.

Case 4

An unmarried female Red Cross worker aged 58 had had attacks of whiteness of all fingers in cold weather for several years. In the winter of 1947–8 her right forefinger became differently affected, the attacks of whiteness becoming more severe and occurring in all climatic conditions, while the finger felt sore and as though there was a constriction around it. Her general health was good and her past history was clear. Her father's fingers used to go dead in his later years.

When we first saw the patient (August, 1948) slight cyanosis was present in all fingers, which were warm. The right forefinger was slightly but definitely swollen, the skin over the middle phalanx was thickened, and it was less mobile than the other fingers. The radial pulses were normal.

The blood pressure was 140/95 in both arms. Nothing abnormal was noted in the skin elsewhere or in other systems. A provisional diagnosis of acrosclerosis was made and she was kept under observation.

During the following winter (1948–9), when the symptoms were more severe, she was given a course of "priscol" (2-benzyl-4,5-imidazoline hydrochloride) without much effect. In May, 1949, she complained of stiffness and swelling of the knees. On examination these exhibited crepitus but no other abnormality. In August further joints became affected—namely, the shoulders and feet—with no abnormality except pain on movement, which was full. In October it was noted that the "arthritis" flitted from joint to joint fairly rapidly, the shoulders often being affected. At this time it was also noted that the right middle finger showed sclerodermatous changes, with swelling of the skin and limitation of movement. The other fingers were less affected but were all swollen and not very mobile. At this stage she was treated with massive salicylate therapy for two months, with some relief of joint pains but without improvement of the fingers.

Her E.S.R. has varied. At the onset of "arthritis" in August, 1949, it was 28 mm. in one hour (Westergren). In September it was 14 mm., and in October (while on salicylates) it was 35 mm. By the end of 1949 she was complaining of vague ill-health, with lassitude as the prominent symptom. She had difficulty in getting on and off buses, could not write or use a typewriter, and had difficulty in feeding herself. There was no dysphagia.

When last seen (September, 1950) there had been progression of the skin changes. All fingers were now affected, being swollen, with typical sclerodermatous skin, so that mobility was impaired. The skin changes also extended over the hands and wrists, stopping fairly abruptly at the lower ends of the forearms. The skin was not affected elsewhere; in particular she differed from the other patients in showing no changes in the face. There was no abnormal pigmentation. Her joint pains continued to flit from joint to joint, but there was no objective evidence, clinical or radiological, of joint involvement. The E.S.R. remained high, being 35 mm. in one hour (Westergren). Some of her tendons showed gross nodularity, best observed in the flexor tendons at the wrists. The nodules were not calcified as judged by radiological appearances. She had no dysphagia or other symptoms of visceral disturbance. A barium swallow showed a normal oesophagus. Screening the chest showed the heart to be slightly enlarged but pulsating normally.

Comment.—The main interest of this case is that the evolution of the disease has been watched from a very early stage, when objective changes were confined to the skin of one finger. There is no indication that the process is becoming inactive. The prior occurrence of Raynaud's phenomena and the nature and distribution of the skin changes are typical of acrosclerosis.

Discussion

This small series of cases supports the view that acrosclerosis is a disease *sui generis*, and that it differs in a number of respects from diffuse scleroderma. All four patients had Raynaud's phenomena preceding or accompanying acrosclerotic changes. Three of them had evidence of visceral involvement, the oesophagus being affected in all three and possibly the heart also in one of them.

In view of the fact that cervical sympathectomy does not relieve the symptoms of acrosclerosis or prevent its evolution, it seems important that every patient with Raynaud's phenomena should be studied with care for evidence of acrosclerosis. With respect to this, it would seem that persistence of swelling of the fingers between attacks or after sympathetic blockage with local analgesics is a sign suggestive of acrosclerosis. Changes in the face are definite confirmatory evidence, but are easily missed unless specifically looked for; for example, our Case 2 was shown as a case of Raynaud's disease at a clinical meeting and no comments were made about her face, nor was the diagnosis questioned. Pigmentation of the skin is another sign to look for, as it is a common manifestation and one which occurs early in the course of the illness.

Joint symptoms are common, so that the disease may be confused with rheumatoid arthritis. The symptoms are of pain and stiffness, which may involve many joints. At the same time the E.S.R. is often raised and the patient suffers from vague ill-health and possibly loss of weight. On the other hand, the joints do not display any objective evidence of rheumatoid arthritis other than limitation of movement, and the radiological appearances are normal.

Summary

Acrosclerosis is a form of scleroderma in which Raynaud's phenomena are common and the skin changes are most evident in the fingers and face. Visceral involvement is also common, the oesophagus being affected most frequently.

Four cases of acrosclerosis are described. All had Raynaud's phenomena. The oesophagus was involved in three.

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At a session devoted to the discussion of inter-university relations during the first congress of the universities of the British Commonwealth to be held after the war a resolution was passed inviting official bodies such as the British Council and the various Governments to provide funds to enable members of teaching staffs on leave to travel within the Commonwealth and to encourage distinguished scholars to visit different parts of the Commonwealth. Travel grants amounting to £5,000 were made by the Council during the first year of the scheme (1949–50), and £7,000 was used in this way the following year. There are three types of award: (*a*) for university teachers on recognized study leave; (*b*) for distinguished scholars and scientists invited by universities for short visits; (*c*) for postgraduate research students holding research grants. Most of those awarded grants under category (*a*) choose to spend most of their time at one or two universities working on a specific piece of research. The second class of grants are mainly to enable experts to meet and talk with younger workers in their own field of studies. About a fortnight is generally spent at each university visited. Fifty-four universities in the Commonwealth have taken part in the scheme by sending or receiving visitors, and the demand for grants is increasing.

ACROSCLEROSIS

BY

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Since Maurice Raynaud first described a condition of intermittent pallor or cyanosis of the extremities, cases have often been diagnosed as Raynaud's disease where pallor, cyanosis, pain, or gangrene of the hands, feet, nose, or ears happens to be present. More often than not such a diagnosis is incorrect. It is therefore considered justifiable to present three cases of acrosclerosis to renew attention to the fact that other diseases have symptoms of a somewhat similar nature to the true Raynaud's disease. Hutchinson (1887) stressed the fact that "Raynaud's phenomenon" was a syndrome occurring in many different conditions, and, more recently, Hunt (1936) has reviewed the many diseases which may resemble but are not Raynaud's disease.

Acrosclerosis is one of those conditions frequently incorrectly diagnosed as Raynaud's disease. True Raynaud's disease consists of symptoms of an *intermittent* nature. The pallor or cyanosis of the extremities is precipitated by cold, and nutritional changes when they occur are limited to changes in the skin; massive gangrene never occurs. All those diseases which may produce the phenomenon simply as a symptom must be excluded before Raynaud's disease is diagnosed.

Aetiology of Acrosclerosis

The most obvious changes in acrosclerosis are found on the face, hands, and feet. Histologically, oedema causes swelling and separation of the collagen bundles of the cutis which eventually become hyalinized. There is cellular infiltration around the vessels, and obliterative sclerosing changes involve the intima. Dermal appendages atrophy (Lewis, 1936).

In view of these changes and the fact that the cases described below have had rheumatoid arthritis or rheumatic endocarditis, it is possible that acrosclerosis may be one of the "diseases of adaptation" (Selye, 1946), and that acrosclerosis might respond to cortisone or A.C.T.H. Diffuse true scleroderma, which is a somewhat similar disease to acrosclerosis, has already been shown to respond to cortisone (McNee, 1950). Should this prove to be the case in acrosclerosis, correct diagnosis would be essential, as no other treatment alters the course of the disease.

Clinical Picture

The majority of published cases have been those of females, symptoms beginning before middle age.

Severe pain in the fingers is almost always present and the fingers become stiff and are often blue in colour, but if the hands are raised the skin becomes white and bloodless. Cold aggravates or initiates colour changes. When the patient attempts to warm the fingers they become deep red and more painful. As the patient learns to avoid cold and as the condition advances, the skin of the fingers becomes a chronic dusky red with waxy white isolated areas at the tips of the fingers. Gradually the colour changes become permanent and are no longer intermittent. The skin becomes thicker and smoother than normal. The fingers appear swollen, giving the skin a stretched, tense, shiny appearance. It is impossible to move the skin, and it seems as if it is adherent to the underlying bones and joints. Small dark areas of superficial gangrene appear on the fingers, frequently at the side of the nail. These spots are extremely painful and either heal slowly, leaving scars, often circular, sometimes linear, and sometimes star-shaped, or infection occurs and a whitlow develops. Such a whitlow is very troublesome and chronic, and results in destruction of soft tissues, the nails, or the phalanges.

Black hard necrotic tissue often builds up below and at the edge of the nail, deforming the tip of the finger. Frequently there is chronic infection below this hardened tissue, and beads of pus may ooze out at the junction of this tissue and the more normal skin. Touching the nail or the hardened necrotic tissue causes great pain. The nail and part of the finger-tip may come away as a slough, leaving a healing, scarred, and shortened finger on which no nail regrows or at most a small beak-shaped nail appears with loose edges which are cracked and turned upwards. In the centre the nail may have ridges of differing thickness.

There is gradual atrophy and absorption of the phalanges, so that each segment of the finger becomes shorter, and sequestra may be discharged from the shortened end of the finger.

Eventually, after many years, some of the fingers become shortened to a level where sufficient blood seems still to flow through the skin and no further destruction or whitlows occur. At this stage the fingers are stiff and straight, but fixed in flexion at the metacarpo-phalangeal joints, so that the hands are of little use. The scars at the end of the shortened fingers still remain acutely painful to touch. Telangiectases may appear on the hands.

The facial appearance is typical. Telangiectases are dotted over the face, being frequently a dusky purple in colour with scattered areas of pale skin here and there, so that the general appearance is one of a high colour but mottled. In these cases the skin is dry, and fine scales may be scraped from different areas. The wrinkles are still well marked, especially around the nose and mouth. The nose becomes narrowed and pinched, with dry areas of skin at the edges of the nares. The mouth is small and the lips are greatly narrowed, so that little or no mucous membrane is visible when the mouth is closed. The hard palate is high and narrow, and if the teeth are still present the upper incisors are prominent, which exaggerates the tightness of the mouth.

In others the skin of the face becomes thick, tense, smooth, and glossy. The telangiectases are then cyanotic and the remainder of the skin is waxy. These changes are more pronounced over the forehead and around the eyes and mouth, where the skin cannot be picked up with the fingers and where the wrinkles disappear. The face assumes a mask-like appearance. The nose and mouth are likewise involved in these cases, so that all these patients resemble each other in general facial appearance.

The skin on other parts of the body may be slightly affected, more so on the feet, arms, and neck. Areas of pigmentation may appear on any part of the body, or the shade of the skin may vary in different regions, making it appear unwashed. The body hair becomes scanty, the patients become flabby, and the abdomen is obese.

A previous history of rheumatoid arthritis or rheumatic fever may be obtained, in which case cardiac disease is likely to be present.

Case 1

A married woman aged 59 was admitted to hospital on May 19, 1947, with left ventricular failure. She had acrosclerosis, which had been diagnosed elsewhere as "Raynaud's disease." At the age of 47 she had been admitted to hospital with rheumatoid arthritis, which affected all the joints of her body; treatment included gold injections, and the condition subsided. Two years later her hands began to turn blue and become cold in cold weather. The fingers became sensitive to slight injury; she often had sores on the knuckles, and whitlows developed easily. The fingers became stiff and gradually flexed at the metacarpophalangeal joints, so that she was unable to grip objects. The repeated whitlows resulted in alteration of the shape of the nails. Her facial appearance changed, and many cyanotic telangiectases developed. Recently she had become very breathless, and had frequent attacks of cardiac asthma.

On examination the face showed multiple cyanotic telangiectases. The skin was cold, thick, and waxy in appearance. The mouth was small and the lips were inverted and cyanosed. The nose was narrow and very firm. There were multiple healed scars on the hands and over the knuckles; many of the scars were star-shaped, consisting of three, four, or five lines radiating from a small depression. The terminal phalanges were shortened; all the nails were deformed and very ridged in the centre, but thin and cracked at the edges. There were a few small recent trophic ulcers surmounted with a thick scab; similar ulcers were present on both elbows, and there was one on the right shoulder. The toes were cold and the skin on the dorsum of the feet was thick and tightly adherent to underlying tissue. The abdomen was pendulous and body hair was absent. There was gross enlargement of the heart (confirmed by *x*-ray examination), and gallop rhythm was present. Electrocardiograms showed incomplete bundle-branch block of the left or common type. B.P. 170/120; W.R. negative.

After one month in hospital she was allowed home, but gradually became more and more breathless and oedematous. Multiple sores appeared on all fingers, becoming septic and very painful. She died three months after leaving hospital.

Case 2

A married woman aged 40 was admitted to hospital on November 29, 1947, with early congestive heart failure. She had acrosclerosis, which had been diagnosed elsewhere as a case of "Raynaud's disease." She gave a history of rheumatic fever when aged 16, and again at 25 years. From birth she had many small cyanosed areas on her face. From childhood her fingers often became cold and cyanosed. Her fingers were very sensitive to injury and easily became septic, causing severe pain. She had frequent whitlows, and once when the middle right finger was poulticed for several days the end separated and came away with the poultice. Over a period of years slowly healing whitlows were accompanied by shortening of the fingers. Since the age of 24 she had had no further whitlows, but the slightest knock to the fingers was very painful. She had very prominent teeth as a young girl, and her mouth was always small. During her first pregnancy her skin became very dark, the pigmentation increasing with her further two pregnancies. Axillary hair disappeared and pubic hair became scanty. Recently she had become breathless on exertion, developed oedema of the ankles, and had palpitations and angina on effort.

Fig. 1.—Case 2. Showing multiple telangiectases on the face, with pinched nose and narrowed tight lips.

On examination multiple telangiectases were seen on the face, the nose was pinched, the mouth small, the lips being stretched over one remaining prominent upper incisor tooth (Fig. 1). The skin on her forehead was thick and wrinkled with difficulty, and over the whole of the face the skin was waxy between the telangiectases. The fingers were stiff, the skin being very thick, hard, cold, and cyanosed. There was shortening of the terminal phalanges of both thumbs and index and middle fingers, with marked deformity of all the remaining nails. There were circular and linear scars on the finger-tips. The skin of the whole body was pigmented, especially on the back of the neck, axillae, and pubic area. Auricular fibrillation due to mitral stenosis with regurgitation was present.

Barium swallow and barium meal showed no evidence of scleroderma. Follow-up 18 months later showed no material change.

Case 3

A married woman aged 46 was admitted to hospital on October 17, 1950, with a previous diagnosis of "Raynaud's disease." When aged 34 she had developed rheumatoid arthritis affecting most of the joints of her body. A year later she was admitted to hospital, where she had treatment, including gold injections, and the arthritis subsided. When she was 38 the fingers began to feel cold and often became deep blue in colour. At other times they were a dull red. These colour changes were more frequent in cold weather. Shortly afterwards the tip of the left fifth finger became black, hard, and very painful. Two weeks later the tip of the finger became worse and finally sloughed off. Since then the other fingers had slowly developed a similar condition. Telangiectases developed on the face, the skin of which was at one time fine and soft. At the age of 43 she had a bilateral cervical sympathectomy, which resulted in the hands becoming warmer, but there was no other change in symptoms, and gradually the hands returned to their original coldness, though the rest of the arms remained warm. More recently she became breathless on exertion.

On examination there were many tiny telangiectases on the face. The skin was dry and mottled. The nose was pinched, with scales around the nares. The lips were contracted and thin, and the opened mouth was small. The fingers and thumb were shortened and deformed (Fig. 2). The skin was dull red, shiny, thick, and adherent to deep tissues. Telangiectases were present. The nails were thin and deformed, and several were raised from the pulp by

Fig. 2.—Case 3. Showing shortened deformed fingers with multiple active sores, gross deformity of the nails, and two large telangiectases at the base of the fingers on the right hand.

thick necrotic tissue from the edges of which pus constantly oozed. There was an odour of gangrene, and the nails were extremely painful to touch. Circular scars covered the ends of the fingers. The body skin was slightly pigmented, the abdomen flabby and prominent; axillary hair was absent, and pubic hair scanty. Mitral stenosis with regurgitation was present.

Discussion

Others (Harbinson, 1904; Johnson and Hedges, 1935) have reported cases in which rheumatoid arthritis preceded the onset of acrosclerosis, but few cases in the literature are described fully enough to show whether or not arthritis is a frequent forerunner of the disease. As the arthritis has involved many joints other than the hands it is unlikely that the pains and stiffness are actually the onset of acrosclerosis.

Hunt (1936) described a "rheumatic" arteritis in which sore throats, arthritis, carditis, or chorea may rapidly be followed by a typical Raynaud's phenomenon, and in severe cases "nutritional changes such as superficial sores at the finger-tips and whitlows may appear," but such cases usually improve rapidly. Hunt also thought that "the vascular symptoms and the rheumatic manifestations suggest a common aetiological factor."

Littler and Canter (1951) are of the opinion that dysfunction of the suprarenal glands is the chief aetiological factor in the pathogenesis of acrosclerosis. They quote Winfield (1904) as obtaining much improvement in a case given suprarenal extract and Schwartz (1917) as improving six cases with pituitary extract.

Two of my cases have had rheumatoid arthritis and two had rheumatic endocarditis. It is suggested that acrosclerosis is a disease of adaptation and would probably respond to cortisone treatment.

Summary

The clinical picture of acrosclerosis is reviewed and three cases are described in detail. It is suggested that it is a disease of adaptation and would respond to cortisone therapy.

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The prefect of Paris issued a decree on June 8 introducing a compulsory medical examination of all taxi-drivers in the capital. Men up to the age of 45 are to be examined every 10 years, and every five years thereafter. The first summons to examination called upon 80 men on September 19, and about half this number attended (*Le Figaro*, September 20). The examination included visual and hearing tests, and the investigation of any propensities to blackouts or nervous troubles. Following these examinations almost all Parisian drivers went on strike for 24 hours in protest, and they have threatened to take further action if the ruling is not modified. Most of the objections are understood to come from the older drivers.

ABACTERIAL CYSTITIS

REPORT OF THREE CASES AND ISOLATION OF A SPIROCHAETE FROM ONE

BY

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Abacterial cystitis is the name given to the syndrome in which there are symptoms and signs of cystitis but no organisms can be demonstrated in the urine by ordinary methods of examination. Characteristically, there is no constitutional upset, but the local symptoms are severe, with dysuria, frequency, and urgency of micturition, and sometimes terminal haematuria; there may or may not be a preceding or coincidental urethritis; cystoscopy reveals an intense cystitis and marked reduction of bladder capacity; and pyelography may show slight dilatation of the ureters and renal pelves. The urine is loaded with pus and sometimes red blood cells, but no organisms can be seen in the stained centrifuged deposit, and no growth is obtained on the usual culture media, either aerobically or anaerobically. Tuberculosis is often suspected, but tubercle bacilli are never found even after guinea-pig inoculation.

Local treatment of the bladder, and the use of urinary antiseptics, sulphonamides, and penicillin have little or no effect. The attack may clear up spontaneously, but in many cases the cystitis persists for months and even for years. After the administration of neoarsphenamine there is always a dramatic response and rapid cure, irrespective of the duration of symptoms. The pyuria disappears, and the bladder capacity, the bladder mucous membrane, the ureters, and the renal pelves all return to normal. Recent reports indicate that arsenoxide ("mapharside") and quinquevalent arsenicals are as effective and that streptomycin and "aureomycin" may also be of value.

It has been suggested by several observers that the causative organism may be a spirochaete. Coutts and Vargas-Zalazar (1946) stated that they found "spirilla of diverse morphology" on dark-ground examination of the urine in five cases and Fieldsend (1947) found "numerous spirillum-like bodies" in one case. These observers did not identify the organism further. It is known that spirochaetes are not uncommonly present even in the healthy genito-urinary tract, and that "spirillum-like bodies" may be seen in degenerating pus. It is difficult, therefore, to determine the significance of such findings in the urines of cases of abacterial cystitis unless the spirochaetes are more exactly defined.

Spirochaetes were seen on dark-ground examination of the centrifuged deposit of urine in three cases of abacterial cystitis recently investigated in the department of venereal diseases at Leeds, and from the urine of one of these cases a spirochaete has been cultured and an attempt made to identify it. Abacterial cystitis is shortly to be the subject of a fuller review by one of us (G. O. H.), and further studies of the spirochaete recently isolated are being undertaken, but a prelimi-

nary report is submitted here. Brief histories of the three cases and bacteriological observations are given.

Case 1

An unmarried man aged 24 reported to us on September 30, 1950. Two years previously he had had an attack of cystitis, with dysuria, frequency, and slight terminal haematuria. The haematuria cleared up in a few days, but the other symptoms and pyuria persisted in spite of taking sulphonamides more or less continuously for about five weeks. He was eventually free of symptoms eight weeks after the onset. There had been no constitutional upset, except for slight malaise and shivering at the onset.

He had no further genito-urinary symptoms in the intervening two years until four days before he reported, when slight dysuria and slight terminal haematuria began. There was a mild constitutional upset on the first day only. On examination he appeared well and had no pyrexia. There was heavy pyuria, but a mid-stream specimen of urine was sterile on culture. Rectal examination revealed no abnormality of the prostate gland or seminal vesicles apart from slight tenderness, and no other evidence of disease was found. All treatment was suspended.

Three days later dysuria and urgency were severe; he was passing urine every 10 to 15 minutes, and was very distressed. There was a profuse blood-stained urethral discharge, and the urine was loaded with pus and blood. Cystoscopy revealed a small-capacity bladder—6–7 oz. (170–200 ml.)—and an acutely congested and oedematous mucous membrane. On October 3 he was given 0.45 g. neoarsphenamine intravenously, and within 24 hours he had considerable relief of symptoms, frequency having been reduced to hourly or longer. A day later there was considerable further improvement, and the pyuria and haematuria were much reduced. On October 6 he was given a second injection of 0.45 g. neoarsphenamine, and four days later, when he had his third injection, he was completely symptom-free, and there were only a few pus cells in the centrifuged deposit of the urine.

Cystoscopy was repeated on October 11. The capacity had increased to 18 oz. (510 ml.) and the inflammation of the mucous membrane was very much reduced. On October 16 there were no pus cells in the centrifuged urine. He was kept under observation at intervals as an out-patient, and remained free of symptoms up to his last visit on March 5, 1951.

Case 2

An unmarried man aged 21 reported on November 14, 1950. He had no previous history of genito-urinary disease. Three weeks previously he noticed slight stickiness of the urinary meatus. A definite urethral discharge developed and was followed by increasing dysuria and frequency and urgency of micturition, but he had not observed any haematuria. At the time of reporting he was passing urine every 5 to 10 minutes during the day and every half-hour during the night, and complained of extreme pain during and after micturition. He had had no constitutional upset, and had been working up to the previous day.

On examination he was found to be very distressed on account of the dysuria and frequency. The oral temperature was 98° F. (36.7° C.). There was a slight muco-purulent urethral discharge, which, on staining, showed numerous pus cells but no organisms, and culture gave a scanty growth of *Staphylococcus aureus, Staph. albus,* and diphtheroids. The urine was very cloudy in both glasses and contained a large amount of pus. Rectal examination revealed no abnormality of the prostate gland or seminal vesicles apart from slight tenderness, and no other evidence of disease was found. Cystoscopy (after meatotomy) disclosed a small-capacity bladder—3–4 oz. (85–114 ml.)—and an acutely congested mucous membrane. Intravenous pyelography revealed a very contracted bladder with coarsened trabeculation. The ureters and renal pelves were not well visualized.

On November 15 he was given 0.06 g. arsenoxide intravenously. There was only slight relief of symptoms by the next day, but a day later the urine was obviously less purulent, and he was able to retain his urine for up to three hours. There was further improvement, and by November 20 he had only slight dysuria (which may have been due to his meatotomy wound), and the urine showed no pus cells on microscopical examination. On this day intravenous pyelography revealed that the bladder was normal.

On the following day he felt unwell, and had pyrexia and some dysuria, and as the urine again contained some pus cells it was suspected that he might have developed a bacterial infection, so sulphonamide treatment was started. A mid-stream specimen of urine taken on that day subsequently grew only a few isolated colonies of *Bact. coli.* All his symptoms subsided within 48 hours, but as the pyuria persisted and red cells reappeared in the urine it was decided to give more arsenic. Culture of a mid-stream specimen of urine at this point showed only a scanty growth of *Staph. albus.*

On November 26 and 28 0.45 g. neoarsphenamine was given. The urine rapidly became free of pus (apart from a few clumps in the first glass, attributed to the healing meatotomy wound) and all symptoms cleared up. On December 8 there were no cells in the centrifuged urinary deposit. He has since been observed at intervals, and remained free of symptoms up till his last visit on February 5, 1951.

Case 3

A married man aged 40 reported on December 4, 1950. While in the Army in 1945 he had an attack of severe dysuria, frequency, and haematuria, associated with a slight urethral discharge. He was admitted to a military hospital and was treated with an alkaline mixture; the symptoms subsided in a few days, although the urine apparently remained cloudy for at least two weeks. He had no further genito-urinary symptoms until three days before reporting, when he began to have dysuria and frequency of micturition (day 20–30 times, night 2–3 times). He had noticed no urethral discharge and no haematuria, and had had no constitutional symptoms.

On examination he was found to have a slight muco-purulent urethral discharge, which, on staining, showed numerous pus cells but no organisms, and no growth was obtained on culture. Dark-ground examination revealed no trichomonads or spirochaetes. The urine was cloudy in the first glass and clear in the second. He was given 600,000 units of procaine penicillin in oil and 5 g. of "sulphatriad" daily for five days as an out-patient. During this time the symptoms and signs gradually subsided, and by December 15 he was symptom-free, the urinary meatus was quite dry, and there were only a few pus cells in the first urine.

On December 18 he stated that he had had severe dysuria and frequency and haematuria for two days, but there had been no constitutional symptoms. He appeared well and the oral temperature was 98.2° F. (36.8° C.). There was a purulent urethral discharge, but no organisms were seen in the stained smear. The urine in both glasses was cloudy and contained a large amount of pus. Cystoscopy was not performed, but intravenous pyelography showed that the bladder, ureters, and renal pelves were normal.

He was given a course of dihydrostreptomycin, 1 g. 8-hourly for seven injections, and 12-hourly for three injections. There was some relief of symptoms within 12 hours of the first injection, and complete relief within 48 hours. The urine rapidly cleared, and after four days there were only scanty pus cells in the centrifuged deposits. He has been observed at intervals since, and was free of symptoms at his last visit on February 26, 1951.

Bacteriological Investigations

Material and Methods

Mid-stream Specimens of Urine.—At the time of admission to hospital in each of the three cases a mid-stream specimen of urine was collected after cleaning the urinary meatus. After centrifugalization the deposit was

examined microscopically (wet film, Gram-stained film, and dark-ground illumination), and inoculated on fresh blood agar and chocolate agar for aerobic and anaerobic culture.

Bladder Specimens of Urine and Biopsy Material.—Cystoscopy was carried out in Cases 1 and 2. In each case, two samples of urine were taken from the bladder (the early flow and the late flow through the cystoscope). Two biopsy specimens were taken from the base of the bladder, near the ureteric orifices, and immediately placed in physiological saline.

Inoculation of Material in Fletcher's Medium.—Specimens, prepared as follows, were inoculated in Fletcher's medium, which is in routine use for culture of leptospira.

Case 1.—In view of the high cellular content of the urine, each of the two specimens of urine obtained at cystoscopy was centrifuged at low speed, and after the sedimentation of the cellular elements the supernatant urine was centrifuged at high speed (about 3,500 r.p.m.) for one and a half hours. The supernatant fluid was siphoned off, and the deposit examined by Gram-stained films and dark-ground illumination and inoculated. The biopsy specimens were triturated with a glass rod and inoculated.

Case 2.—Both specimens of urine obtained at cystoscopy were examined microscopically and inoculated after slow centrifugalization only, and the biopsy material was treated as in Case 1.

Case 3.—Two specimens of mid-stream urine (the early and late flow) were inoculated without preliminary centrifugalization.

Inoculation of Guinea-pigs.—In each case equal parts of the two specimens of urine were mixed and injected into two guinea-pigs, one intraperitoneally and one subcutaneously. In the first two cases centrifuged deposits were injected, and in the third whole urine.

Results

Mid-stream Specimens of Urine.—In each case there was a large quantity of pus with a variable number of red blood cells, the deposit constituting up to about a tenth of the volume of urine. No organisms were seen in the stained films, and all cultures remained sterile. Actively motile spirochaetes were seen on dark-ground illumination in all three cases, but not in the actual specimen used for inoculation in Case 3.

Inoculations in Fletcher's Medium.—Dark-ground examination of the cultures after incubation at 30° C. for three days revealed scanty spirochaetes in those of the late-flow urine and biopsy material in Case 1. The culture of the early-flow urine in this case, and of all the specimens in the other two cases, remained sterile.

Subcultures were made of the growth obtained in Case 1. Preliminary studies showed that the spirochaete morphologically resembled leptospira, and electron microscope photography revealed that it was identical morphologically with *L. canicola* and *L. icterohaemorrhagiae* grown under identical conditions. Attempts are being made to identify it further.

Inoculated Guinea-pigs.—Case 1: both guinea-pigs were killed after eight weeks, and no evidence of disease was found. *Case 2:* both guinea-pigs died of intercurrent infection (bronchopneumonia) after six weeks. *Case 3:* both guinea-pigs were killed after 17 weeks; no evidence of disease was found.

Discussion

There are several possible explanations of the fact that, although actively motile spirochaetes were seen in the urine of all three cases, they were from only one case. Spirochaetes are notoriously difficult to grow, especially in primary culture, and the necessary element of luck may have been present in the first case. Spirochaetes were seen on dark-ground illumination in only two of the three specimens used for inoculation. Different batches of media were used for each case. Apart from the biopsy specimens, the preparation of the material for inoculation was different in each case.

Obviously the evidence presented is not adequate to prove that the spirochaete isolated is the causative organism of the syndrome described, and further investigations are required. It is, however, a very unusual finding, which may contribute to the elucidation of the cause of abacterial cystitis and extend the knowledge of the leptospira.

Summary

A brief description of the main features of the syndrome of abacterial cystitis is given, and three case histories are quoted. Actively motile spirochaetes were seen in the urine of each of these three cases. A spirochaete morphologically closely resembling leptospira was grown from the urine of one of them, but not from the other two.

We are indebted to Professor J. W. McLeod, F.R.S., for advice and encouragement, and to Mr. H. D. Moore, F.R.C.S., for carrying out the cystoscopic examinations.

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THE VALUE OF EXTERNAL CEPHALIC VERSION UNDER ANAESTHESIA

BY

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External cephalic version without anaesthesia is an established procedure forming an important part of antenatal care in preventing the foetal loss and dystocia associated with a breech delivery. The same cannot be said for version under anaesthesia, and the published results of this procedure are few. White and Flew (1933), in reporting 92 cases, stressed the dangers of vaginal bleeding which occurred in six of their patients. Wrigley (1934) reported 76 cases with successful version in 45 and assessed the foetal mortality at 13%. This figure seems surprisingly high by modern standards, but it compared favourably with the foetal death rate of 28% for breech delivery given in the same paper. Newell (1941) recorded 48 cases with 18 successes. Peel and Clayton (1948) reported a success rate of 87% in 172 primiparae with four foetal deaths due to version under anaesthesia and a success rate of 89% in 64 multigravidae with no foetal mortality attributable to the version. Their total foetal mortality due to version under anaesthesia was 1.7% in a total of 236 cases (253 attempts), but five infants were subsequently lost during delivery as a breech or a vertex.

The usually quoted foetal mortality of breech delivery is about 10% (Peel and Clayton, 1948; Munro Kerr and Chassar Moir, 1949; Drew-Smythe, 1950), although Dieckmann (1946) gives a corrected mortality of 4.2%, Seeley (1949) a figure of 3.5% for full-term infants, and Cox (1950) a corrected mortality of 4.98%. In an endeavour to prevent this unnecessary infant loss which may be attributed solely to a breech delivery, and to transform the abnormal to the normal, it has been the practice at the Central Middlesex Hospital to perform version under anaesthesia when attempted version without anaesthesia has been unsuccessful.

The object of this paper is to show the results of a series of cases of version under anaesthesia and to evaluate whether these results justify its use as a routine antenatal procedure. The questions to be answered are: Is there an unnecessary risk to the mother and foetus by using anaesthesia when previous attempts without it have failed, and is its use justified by the number of successes obtained? If it can be shown that the risks are slight, and that the foetal mortality is materially lower than that of breech delivery, a strong case will have been established for its more widespread adoption.

The essential advantage of anaesthesia is that it overcomes the common factors preventing version in the antenatal clinic—namely, resistance of the abdominal muscles and, to a lesser extent, the contractions of the uterus. We do not agree with repeated attempts at version under anaesthesia, and, if a successful version cannot be performed with anaesthesia once, the patient is allowed to have a breech delivery, or a caesarean section is performed at term if indicated.

The following are regarded as contraindications to version: multiple pregnancy, suspected placenta praevia, toxaemia, previous classical caesarean section, and where an elective caesarean section is to be performed at term. Deep engagement of extended breeches when the buttocks reach the ischial spines are unsuitable cases, as also are those in which a foetal abnormality such as hydrocephalus has already been diagnosed. Munro Kerr and Chassar Moir (1949) think that marked hypertension contraindicates version, and we agree with that view. We do not regard elderly primigravidae as unsuitable cases.

Technique

The patient is admitted to hospital and detained for the night following the version. Premedication consists of "omnopon," 1/3 gr. (22 mg.), with scopolamine, 1/150 gr. (0.43 mg.). Various anaesthetic agents have been used—thiopentone, thiopentone with ether, "trilene," or cyclopropane, and recently thiopentone with 1 or 2 ml. of gallamine triethiodide ("flaxedil"). Unless the version is completed within one minute of the full dose of thiopentone being given, experience has shown that further attempts are useless until the anaesthetic is deepened, the essential feature of the anaesthesia being adequate muscular relaxation. The Trendelenburg position is not used. The first step is to displace the breech from the pelvic brim to the iliac fossa on the side the back is lying, and in some cases this can be done only by disengaging the breech per vaginam. The head is then flexed and by firm tangential pressure the infant is brought into the transverse. Time is then given for the uterus to relax, still maintaining a steady pressure, and soon the head slips downwards, thus completing the operation. In some cases turning the baby in the opposite direction will succeed when flexing of the foetal head and trunk have failed. Jerky or forceful movements are never used.

We find that the common left or right sacro-anterior positions are often transformed into posterior positions of the vertex, and consequently the deflexed head remains high immediately after the version. When the patient is seen at the antenatal clinic one week later the head has usually gone down and an anterior or lateral position has been assumed by the foetus. Immediately after the version the foetal heart is counted, and in some cases it has slowed but after a minute or so resumes its normal rhythm. We have not found it necessary to turn the foetus back to a breech because of irregularity or alarming bradycardia of the foetal heart. Pads and binders are then applied and the foetal position and heart are checked again before the patient is allowed home next morning.

Clinical Results

The following figures represent an analysis of the total number of cases of version under anaesthesia performed at the Central Middlesex Hospital from 1944 to 1950. It must be emphasized that all the cases have had at least one, and often more than one, attempt at external version without anaesthesia, and thus the present series represents only the most difficult cases. The total figures for both primiparae and multigravidae are set out in Table I. The 11 stillbirths and neonatal deaths include five from foetal abnormalities and one from pre-eclamptic toxaemia which developed after the version.

TABLE I.—*Results of Whole Series*

Total No. of Cases	Maternal Mortality	Version Successful	Stillbirths and Neonatal Deaths	Foetal Mortality Due to Version
214	Nil	174 (81·3%)	11	3 (1·4%)

Table II represents the detailed analysis of the primigravid patients, and for the purposes of this investigation patients who have had one previous miscarriage have been included with the primigravidae.

TABLE II.—*Analysis of Primigravid Patients*

Total No.	Successes	Stillbirths and Neonatal Deaths	Foetal Loss Due to Version	Delivery			
				Normal	Forceps	Breech	Caesarean Section
135	105 (77·7%)	6	Nil	84	18	23	10

Of the six foetal deaths in the primigravid patients three were neonatal deaths due to spina bifida with hydrocephalus. The fourth case developed severe pre-eclamptic toxaemia of pregnancy for which a surgical induction was performed. This patient had an inert first stage of labour lasting 48 hours, but the foetal heart was quite strong and regular till the late first stage, when it suddenly ceased. An 8 lb. 7 oz. (3.8 kg.) stillborn infant was subsequently delivered by forceps. We consider that the well-developed pre-eclamptic toxaemia associated with a long first stage of labour was responsible for this foetal death. The fifth case had a successful version at 38 weeks on March 12, 1948, and was seen regularly at the antenatal clinic until April 7, the foetal heart being heard on every occasion. The patient

was admitted in labour on April 12 with the membranes intact, but she had not felt any foetal movements during the previous 48 hours. She had a normal delivery in 13 hours 30 minutes, and a stillborn infant weighing 7 lb. 14 oz. (3.6 kg.), length 22½ in. (57 cm.), was delivered. The placenta was extensively infarcted, and as the patient was 23 days overdue it was considered that this intrauterine foetal death was attributable to placental insufficiency and post-maturity. The sixth case had a normal delivery, but the midwife in charge had considerable difficulty in delivering the shoulders of a 9 lb. (4.1 kg.) infant which could not be resuscitated. This foetal death must be attributed to the delay in delivering the shoulders.

Table III represents the detailed analysis of the multigravid patients. Two of the foetal deaths were due to perforations for hydrocephalus. The other three cases are reported more fully.

TABLE III.—*Analysis of Multigravid Patients*

Total No.	Successes	Stillbirths and Neonatal Deaths	Foetal Loss Due to Version	Delivery			
				Normal	Forceps	Breech	Caesarean Section
79	69 (87·3%)	5	3 (3·7%)	67	2	8	2

Case A.—Attempted version was made at 36 weeks on April 21, 1949, and the foetal heart was heard the next day. The patient was admitted in labour on April 24 with the membranes intact, but the foetal heart could not be heard; vaginal bleeding had not occurred between the attempted version and admission to hospital. The patient had an assisted breech delivery of a 5 lb. 15 oz. (2.7 kg.) stillborn infant. The reason for this intrauterine foetal death is not clear, but it must be attributed to the attempted version.

Case B.—This patient had a particularly bad obstetric history consisting of an abortion in 1935; a breech delivery in 1936 of a 6½ lb. (2.95 kg.) infant who died from jaundice on the third day; further abortions at three months in 1937 and 1938; and five-month abortions in 1939 and 1940. In 1942 she had a normal breech delivery of a 6 lb. 6 oz. (2.9 kg.) baby which is alive and well. In 1943 she became pregnant again but developed massive oedema of both legs without hypertension, and an intrauterine foetal death occurred at 35 weeks. She was Rh-positive, her W.R. was negative. In her ninth pregnancy external version under anaesthesia on January 18, 1946, at 35 weeks proved unsuccessful. The next day she had a slight "show" which did not recur or affect the foetal heart. She was next seen at the antenatal clinic on January 23, when the foetal heart was again recorded, but in the meantime she had developed oedema of the legs. She went into labour on January 31, having felt no foetal movements for the previous 48 hours, and a stillborn infant was delivered. She thus repeated the events of her previous pregnancy—namely, the rapid onset of oedema at 35 weeks followed by an intrauterine foetal death. This patient was clearly predisposed to unstable pregnancies and had already had two previous breech deliveries. On mature consideration we conclude that the attempted version under anaesthesia was not justified. In spite of the oedema this case has been included as a foetal death due to version in view of the vaginal haemorrhage.

Case C.—This case of a woman aged 40, who had a ruptured uterus due to version under anaesthesia, illustrates one of the possible dangers of this procedure. Version under anaesthesia was undertaken on April 21, 1949, when she was 36 weeks pregnant; vaginal bleeding did not occur during the operation. In the night, however, she complained of abdominal pain, and the uterus was very tense, tender, and irregular in contour. There was a little dark red loss per vaginam. Radiographs showed the foetus partly through the uterus on the left side of the posterior fundal wall. Laparotomy was performed and the foetus was found protruding through a vertical rent on the posterior surface of the uterus; 10 oz. (284 ml.) of dark blood was present in the peritoneal cavity. The foetus, which weighed 5 lb. 2½ oz. (2.3 kg.), was delivered from the uterus followed by the placenta and membranes, the rupture was repaired, and the patient made an uneventful recovery. At operation no abnormality was seen to account for the rupture.

Table IV shows the number of attempted versions at the various stages of pregnancy, with their corresponding successes.

TABLE IV

Weeks	No. Performed	No. Successful	Weeks	No. Performed	No. Successful
34	25	23	37	54	44
35	26	21	38	24	12
36	79	69	39, 40	6	5

The caesarean section rate for the series was 5.6%, only 12 sections being done from a potential number of 214 breeches. Bicornate and subseptate uteri accounted for three of the primigravid sections; two were unsuccessful versions with contracted pelves; two were for breeches with inertia; one was performed for an unsuccessful version followed by pre-eclampsia; one was performed on a successful version, as a soft tumour in the pelvis prevented engagement of the head; and one was a successful version followed by an unsuccessful trial of labour for disproportion. One of the two multigravid sections was performed for lateral placenta praevia and the other because of a ruptured uterus (Case C.).

Complications

Apart from Cases A and B, reported above, premature labour due to the version occurred in only seven of our cases, with no foetal loss. The cord came down with the breech in three unsuccessful cases and prolapsed in one vertex presentation, all without foetal loss; there were no compound presentations. Prolapse of the cord is always possible after version, whether the infant has been turned or not, and we endorse the advice of Munro Kerr and Chassar Moir to perform a vaginal examination early in labour to determine if the cord is presenting.

Two cases returned to a breech presentation after a successful version and have therefore been included among the unsuccessful cases. One case, with a contracted pelvis, returned to a breech, but was turned again under a second anaesthetic and subsequently had a trial of labour with a normal delivery of a 6 lb. 2½ oz. (2.8 kg.) baby.

A small number of vaginal haemorrhages occurred during the version, the loss never being severe. We do not consider such loss of serious import, providing it is seen and the operation immediately stopped.

Extended legs occurred in 79.2% of cases *x*-rayed before using anaesthesia, while of the cases subsequently having a breech delivery the legs were extended in 87.5%. We therefore believe that if the legs are flexed external version should succeed.

Discussion

In assessing the foetal mortality the infant loss due to the version as well as those subsequently lost in labour

as a breech or a vertex must be taken into account when comparing these results with a series of breech deliveries. Of previous publications on the foetal risk in breech delivery one of the most important is by Lloyd Woodrow Cox (1950), of Liverpool, whose figures must be regarded as a challenge to the low foetal risk of version under anaesthesia. Cox gives a foetal mortality rate for uncomplicated breech delivery in Liverpool for the past 16 years as 4.98%, and 3.2% for the past five years. We lost six infants from a total of 214, three due to version, one from toxaemia, one from post-maturity, and one from shoulder dystocia. If we regard the death from toxaemia as "complicated" this gives the final foetal mortality as 2.3%, which compares favourably with the Liverpool figures. Cox has also shown that for infants over 7½ lb. (3.4 kg.) the foetal mortality for a breech delivery is 10%; in our series 30.3% of the infants born weighed over 7½ lb. (3.4 kg.).

It is clear that in achieving the excellent figures for breech delivery in Liverpool the caesarean section rate is exceptionally high. Version under anaesthesia definitely lowers the caesarean section rate, as a trial of labour may be safely conducted in suspected disproportion, and this usually results in a normal or forceps delivery. Moreover, the majority of breeches can be turned easily in the antenatal clinic without anaesthesia and we can see no reason why the same success cannot be achieved as when anaesthesia is used; indeed, in all probability it will be greater. We do not agree, therefore, with the Liverpool school, who make "no particular effort to avoid this (breech) presentation" (Cox, 1950), but hold to the view that prevention is better than cure, and it is submitted that the results of this series justify that view.

It might be concluded from these figures that version under anaesthesia should be largely confined to primigravidae, and we incline to this view. We believe that it should be possible to attain an 80% success rate, with a foetal mortality of *nil* or thereabouts attributable to the version, and that the results so obtained cannot be equalled for breech deliveries in primigravid patients in whom version using anaesthesia has not been attempted. Furthermore, it is safe for a version to be performed and for the mother to have her baby at home under the care of her family doctor, thus dispensing with admission to hospital necessitated by a primigravid breech delivery.

Those hospitals that have a high incidence of primigravid breech deliveries and in which version under anaesthesia is not practised should consider whether by adopting this procedure they can reduce unnecessary stillbirth and neonatal deaths.

Summary

An analysis is given of 214 cases of external cephalic version under anaesthesia. The foetal mortality rate due to the version was 1.4%. Two cases were subsequently lost in labour, giving a final corrected foetal mortality rate of 2.3%. Previous attempts at version without anaesthesia had been unsuccessful in all cases. Version with anaesthesia succeeded in 81.3%.

It is concluded that the number of successes obtained and the low foetal risk justify using this procedure as a routine antenatal measure, thus reducing the stillbirth and neonatal wastage from breech deliveries.

We should like to express our thanks to Miss M. A. M. Bigby for permission to include her cases.

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MASS B.C.G. VACCINATION IN A BRITISH COLONY

BY

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In Singapore resistance to disease was greatly reduced during the years of enemy occupation, 1942–5. This was particularly true of pulmonary tuberculosis. The local population were deprived of rice, their staple food, and local agriculture was quite incapable of producing an adequate substitute. In addition to starvation, heavy labour conditions, crowded living accommodation, mental depression, and fear all helped to increase the incidence of disease.

In August, 1948, the Health Department in H.M. Naval Base inaugurated a medical service in the Dockyard Asian School, which has a roll of between 500 and 600 children. The naval medical officer of health felt that regular medical examinations of these Asian children would be of use in the early detection of malnutrition, skeletal maldevelopments, and clinical conditions such as tuberculosis, and also that these children should be educated in the elements of health and hygiene.

When the school medical service had been established on a regular basis it was decided to submit the children to a tuberculin test, using the diagnostic jelly of Messrs. Allen and Hanburys. This contains 95% of old tuberculin. The technique employed was to clean with ether an area of skin on the lateral side of the arm. The test and the control jellies were applied to this area in the shape of a diamond, the lower V of which was the test jelly, and the area was covered with a piece of adhesive plaster. There was no preliminary rubbing of the skin with flourpaper. Tests were read at three days and daily until seven days after testing. A positive result was recorded only when there was a reaction of at least five papules or vesicles, or when a raised weal showed on the skin. There were no reactions from the control jelly. Of 574 children tested in this way 52 were not read. Of the remainder, 47 (9%) were positive-reactors and 475 (91%) were negative. The positive-reactors were then submitted to a chest *x*-ray examination. None showed evidence of active disease, but all had healed lesions.

Discussion of our results with the Singapore Anti-Tuberculosis Association led to their offer of co-operation if we wished to avail ourselves of B.C.G. vaccination. It was arranged that they would provide the vaccine free of charge and would instruct us in the technique

of vaccination, while the Naval Health Department would carry out the preliminary testing, do the bulk of the vaccinations, and retest the children some eight weeks later. It was also decided to widen the scope of the operation by including all the Asian children within the naval base whose parents wished to have them vaccinated. The response far exceeded anything we had hoped for.

Preliminary Tuberculin Test

Working on seven afternoons, we applied the tuberculin-jelly test to 2,684 children, whose ages ranged from 2 months to 16 years. The following modified technique was used. An area of skin between the scapulae was cleaned carefully with ether, and then stroked firmly with fine flourpaper. The jelly was placed on the skin so treated in the form of a V, and the area was then covered with a piece of adhesive plaster 2 by 1 in. (5 by 2.5 cm.). We did not use the control jelly supplied, as we had had no reactions with this jelly during our previous tests. To lessen the work, and because we were not in any sense carrying out a controlled experiment, we felt justified in discarding it. The parents were warned not to allow the patch to get wet during the next 48 hours, and were instructed to bring the children back again after 72 hours to have the test read.

Results of Tuberculin-testing

The results of the test are given in Table I.

TABLE I.—*Results of Preliminary Tuberculin Test*

Age in Years	No. Tested	No. Positive	No. Negative	Result Not Known	Percentage Positive of Known Results
0–	468	18	426	24	4·1
2–	526	38	463	25	7·6
4–	302	58	228	16	20·3
6–	312	82	215	15	27·6
8–	376	138	219	19	38·7
10–	358	139	202	17	40·8
12–	254	115	126	13	47·7
14–	81	33	44	4	42·9
16+	7	3	3	1	50·0
Total	2,684	624	1,926	134	24·50

We read the tests at the end of the third day only, not daily to the seventh day as recommended by the manufacturers, as in the first series of tests we had found that children who were negative on the third day never afterwards became positive when read daily. To ensure uniformity in estimating what constituted a positive reaction, the naval medical officer of health alone read the results. Among the 2,684 children tested were 498 dockyard schoolchildren who had been included in our first series of tests. With the flourpaper technique the results were: positive 215 (43.2%), negative 283 (56.8%); to be contrasted with 9% and 91% respectively with the simpler technique. The relationship between positivity and three-year age groups is shown in Table II, from which it will be seen that there are no very marked differences between one race and another.

In absolute numbers, and in all races, there is a marked preponderance of children of ages up to and including 3 years over the groups which immediately follow. There were 994 at ages 0 to 3 years inclusive, compared with 614 at ages between 4 and 7 years inclusive. This may be due to chance, but possibly indicates excessive mortality among babies and young children during the Japanese occupation. Positive reactors were found in every age group and the positive proportion of each three-year group rose steadily with age.

The B.C.G. Vaccination

There was an unavoidable delay of 11 weeks between the completion of the tuberculin-testing and the first vaccination. This interval must prejudice the conversion figures, since a number of negative reactors may have become positive in the interim. The number doing so is, however, probably quite small—1.1% as calculated by working out the fractional increase for 11 weeks on the highest percentage increase in the proportion positive in Table II—namely, 15.3% from the 3– to the 6– age group. The vaccine was made up for use by alternately filling and withdrawing from the ampoule 2 ml. of sterile distilled water. The dried vaccine readily became suspended after 15 to 20 charges and discharges of the syringe. An area of skin on the lateral side of the arm was cleaned first with spirit and then with ether. Three drops of vaccine suspension were placed separately on the area of cleaned skin and were spread out. A cruciate scratch was made through each drop with a triangular, straight surgical needle. This scratch was made boldly so as to draw a very little blood. With the side of the needle the vaccine (usually admixed with a little blood) was spread up and down through the three incisions. When the vaccine had dried a piece of adhesive plaster was used to cover the area of vaccination.

We employed four teams of two persons. A team was able to deal with 60 children an hour, and our daily average of vaccinations was about 700. Of the 1,926 children who were found to be tuberculin-negative, we succeeded in locating and vaccinating 1,809. The other 117 had left the naval base in the period between testing and vaccination. There were no adverse reactions of any kind after vaccination. Those who became positive as a result of the vaccination often showed a reaction at the site analogous to that seen after successful vaccination against smallpox. There were no slow-healing ulcers of the kind described in the literature.

TABLE II.—*Results of Preliminary Tuberculin Test*

Age in Years	Malays				Chinese				Indians				Total (All Races)			
	No. Tested	No. Pos.	No. Neg.	% Positive of Known Results	No. Tested	No. Pos.	No. Neg.	% Positive of Known Results	No. Tested	No. Pos.	No. Neg.	% Positive of Known Results	No. Tested	No. Pos.	No. Neg.	% Positive of Known Results
0–	160	10	150	6·3	185	4	181	2·2	391	23	368	5·9	736	37	699	5·0
3–	80	13	67	16·3	225	29	196	12·9	188	35	153	18·6	493	77	416	15·6
6–	61	16	45	26·2	228	75	153	32·9	186	56	130	30·1	475	147	328	30·9
9–	60	19	41	31·7	227	92	135	40·5	230	98	132	42·6	517	209	308	40·4
12+	42	23	19	54·8	159	81	78	50·9	124	47	77	37·9	325	151	174	46·5
Total	403	81	322	20·1	1,024	281	743	27·4	1,119	259	860	23·1	2,546	621	1,925	24·4

N.B.—Four Eurasian children have not been included.

Results of Vaccination

The tuberculin-testing of the vaccinated children to establish the conversion rate was begun eight weeks after the vaccination (the period recommended by the Pasteur Institute). Of the 1,809 children vaccinated we were able to locate and retest only 1,419, the other 390 having disappeared from the base. It must be explained that throughout the whole operation some children fell away at each step of the proceedings.

The same technique of tuberculin-testing was used, and of 1,419 tested, 743 (52.4%) were positive and 676 (47.6%) negative. If we regard as reasonable the supposition that, of the 390 children vaccinated but not subsequently retested, 52.4% also become positive, we ended our campaign with a total of 743+204=947 children protected against tuberculosis. The results are shown in Tables III and IV.

TABLE III.—*Retesting of Vaccinated Children*

Age in Years	No. Tested	No. Positive	No. Negative	Result Unknown	Percentage Positive of Known Results
0–	394	147	173	74	45·9
2–	435	182	181	72	50·2
4–	211	82	93	36	46·8
6–	204	82	82	40	50·0
8–	205	85	65	55	56·6
10–	196	89	42	65	67·9
12+	164	76	40	48	65·5
Total	1,809	743	676	390	52·4

TABLE IV.—*Retesting of Vaccinated Children*

Age in Years	Malays					Chinese					Indians					All Races				
	No. Tested	No. Pos.	No. Neg.	Result Not Known	% Positive of Known Results	No. Tested	No. Pos.	No. Neg.	Result Not Known	% Positive of Known Results	No. Tested	No. Pos.	No. Neg.	Result Not Known	% Positive of Known Results	No. Tested	No. Pos.	No. Neg.	Result Not Known	% Positive of Known Results
0	133	44	39	50	52·0	176	76	73	27	51·0	343	125	171	47	48·8	653*	246*	283	124	46·6
3–	56	27	11	18	71·0	188	87	83	18	51·2	143	51	70	22	42·1	387	165	164	58	50·0
6–	41	12	15	14	44·5	146	69	55	22	55·6	122	47	41	34	53·4	309	128	111	70	53·5
9–	40	10	5	25	66·6	133	70	33	30	68·0	123	48	40	35	54·5	296	128	78	90	62·1
12+	17	8	4	5	66·6	76	44	19	13	70·0	71	24	17	30	58·5	164	76	40	48	65·5
Total	287	101	74	112	57·8	719	346	263	110	56 8	802	295	339	168	45·6	1,809	743	676	390	52·3

* 1 Eurasian child added.

The conversion rate was admittedly disappointing. Rydén (1946) reports 99% reactors from a series of 7,475 vaccinated. Only 3 of the 65 non-reactors failed to become positive after revaccination. Birkhaug (1944), in his series, obtained 97 to 98% reactors after four to six weeks. He used a multiple-puncture technique. Hertzberg (1946) reports that of 13,515 vaccinations in Norway during 1943 95% became reactors. From these figures, and from other sources, we must infer that our reactor percentage was a poor result for the work done. We think there are four reasons for this: (*a*) The dried vaccine may not always have been completely suspended, and some may have been left in the ampoule. We found in a subsequent series of vaccinations on European children that great care had to be taken to ensure complete suspension. (*b*) The cruciate scratches were often not made deep enough. (*c*) We felt certain that with a large number of the children the vaccine was not allowed to dry properly before the site was covered with gauze and plaster. We also suspected that many mothers wiped away the vaccine from their children's arms—a normal action when the vaccine was blood-stained. The more or less steady increase of the proportion positive with age (Tables III and IV) tends to confirm this suspicion. (*d*) The vaccine may not have been rubbed into the arms thoroughly enough with the edge of the needle. The faults sprang from inexperience in vaccinating and (more especially) from trying to do too many children at one time.

Summary

The high incidence of tuberculosis amongst Asian children is noted, and some causes are suggested.

The steps in tuberculin-testing a large number of children of all ages are given; and the age grouping of the results is discussed.

The vaccination of 1,809 children of all ages with dried B.C.G. vaccine is described in detail.

The results of this vaccination, found to be a change from a negative to a positive tuberculin reaction in 743 children, are discussed, and reasons are suggested why this conversion rate was not higher.

I am grateful to Dr. G. H. Garlick and Dr. A. Bardsley, of the Singapore Anti-Tuberculosis Association, for the immense help they gave so willingly; to my wife and other European ladies who helped in the testing and vaccinating, often under considerable difficulties; to the Captain of the Dockyard and the Officer Commanding, Royal Naval Police, for their interest and help; to the staff of the Naval Health Department, Singapore, who (both Asian and European) worked so hard to make the campaign a success; and to Dr. John Knowelden, of the Department of Medical Statistics, London School of Hygiene and Tropical Medicine, for his invaluable advice. I wish to acknowledge with thanks the permission of the Medical Director-General of the Navy to submit this paper for publication.

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A warning to parents to keep medicines locked up and out of the reach of children was recently given by the Preston district coroner. Recording a verdict of "Accidental Death" on a 2-year-old child who died from strychnine poisoning as a result of swallowing tablets prescribed for her mother, the coroner said he wanted to make one or two observations on the case. The pills had been kept on the sideboard, behind the clock, presumably out of the child's way, but she had found them, opened the box, told her mother she was eating toffee, and had swallowed the pills, no doubt thinking they were toffees. He said he wanted to emphasize the fact that nowadays there were going into the homes of many people medicines which were poisonous. They were not poisonous if taken in accordance with the doctor's prescription, but dangerous if not so taken, and extremely dangerous to children. He suggested that boxes of toxic pills should be labelled dangerous unless used strictly in accordance with the doctor's prescription, and also that they should be kept out of the way of children.

A COUNTY B.C.G. CAMPAIGN

BY

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County Sligo has a population of 63,000, and, with the exception of the town of Sligo (population 13,000) and two small towns of 1,000 each, is almost completely rural. There are few industries in the county, the people mostly being divided between agriculture and trade. For the statistical purposes of this article the town of Sligo only has been regarded as urban; the rest of the county is classified as rural.

In common with the other counties of Ireland, Co. Sligo's tuberculosis death rate has been high in comparison with neighbouring countries and those of the Continent, usually averaging around 1 per 1,000. Nevertheless we have resigned ourselves to the fact that for some years our county has had a bad reputation as being a hotbed of tuberculosis: at a London University M.A. examination some years ago one of the subjects for discussion was the abnormally high death rate from tuberculosis prevailing in Co. Sligo.

When, therefore, the National B.C.G. Committee, in January, 1950, made an offer to co-operate with us in Co. Sligo in starting a large-scale tuberculin-testing survey with a view to the introduction of a B.C.G. anti-tuberculosis campaign, it was with some eagerness and still more trepidation that we accepted.

The National B.C.G. Committee was formed in July, 1949, under Government auspices. Its object is to put on a national basis the work which owes its origin to the pioneering spirit of Dr. Dorothy Price, who since 1947 has been successfully vaccinating with B.C.G. at St. Ultan's Hospital, Dublin. Through her years of campaigning and her study of the schemes in use in Sweden, Norway, and Denmark, she finally persuaded the Government to sponsor a national campaign in this country to make B.C.G. vaccination available everywhere.

On its first visit to Co. Sligo, the committee adopted the safer but slower procedure of testing with Moro's ointment, then with 1/1000 old tuberculin, and finally with 1/100 O.T. Even then the negative reactors are not vaccinated lest they should be incubating the disease, but after an interval of six weeks they receive a second maximum test dose of 1/100 O.T., and if this is again negative they receive their B.C.G. vaccination.

We had agreed to start work on three orphanages in the county, and we had also asked a number of medical and other business and professional persons to submit their children for testing with the object of setting a good example for the local population. These numbered 110, and we added 48 contacts of our own tuberculous and suspected tuberculous patients.

A few weeks previous to this we had removed to our local hospital from one of those orphanages a child of 10 with positive sputum, so we were expecting a high degree of infection there, and our fears were realized on finding that, of 171 children from 2 to 16 years, 127 were positive to Moro's test, and of the 44 negative children 24 were positive to 1/1000 O.T. (none of the remaining 20 were positive to 1/100). On subsequent *x*-ray examination 10% of those reactors were found to have had a recent primary complex (most of them symptomless); but further investigation by gastric lavage, etc., revealed no other open case, and since this survey and the B.C.G. vaccinations no further trouble has arisen there.

The relative findings for the remaining three centres were as shown in Table I.

TABLE I

	Moro Test		O.T. 1/1,000		O.T. 1/100		Total Pos.	% Pos.
	No.	Pos.	No.	Pos.	No.	Pos.		
Orphanage 2 ..	93	26	67	5	62	1	32	34
3 ..	107	29	78	6	72	1	36	33
Public centre ..	158	15	142	3	127	—	18	11

Excluding No. 1 Orphanage, which was regarded as exceptional, this result was considered satisfactory, and it was arranged that when the time for the vaccination of the first batch was due a second batch would be ready.

This second batch consisted of four secondary and six primary schools, all situated in the town of Sligo. The B.C.G. Committee decided that the slower method should be again adopted, as it was not certain what amount of infection might be encountered.

In all, 1,715 children submitted themselves for examination, and of these 180 were positive to Moro's test, while 108 failed to present themselves for reading; 1,427 were tested with 1/1000 O.T., 162 proving positive and 59 being absent; and of the 1,206 who returned for the final test of 1/100 O.T. 59 were positive, while 55 were absent from reading. This matter of absenteeism from result-reading has complicated the computation of percentages, but the best that could be done to overcome this was to assume that the same percentage of positives would have occurred in the absentees as in those who returned, and to add this percentage to the total of known positives. Thus there were 401 positive reactors, which is 23.3% of 1,715; and as 23.3% of the 222 absentees is 51, we are taking the total positives as being 452. This gives a total proportion of positives as 26.3%. The total figures for this batch are shown in Table II.

TABLE II

Moro Test			1/1000 O.T. Test			1/100 O.T. Test			Totals		% Pos.
No.	Pos.	Abs.	No.	Pos.	Abs.	No.	Pos.	Abs.	Pos.	Abs.	
1,715	180	108	1,427	162	59	1,206	59	55	401+51	222	26·3

When the committee is satisfied that a group or a district is relatively free from infection and that there is little likelihood of children being incubators of infection, a bolder and quicker method is adopted and the entire procedure of testing and vaccination is completed in one week. On Monday the ointment is used on children up to 15 years, or 1/5000 O.T. on those over that age. On Wednesday all non-reactors are tested with 1/1000 O.T., and on Friday all the negative reactors are vaccinated. On Tuesday, Thursday, and Saturday another group of children is completed in the same way. Thus much time and "needling" are saved and this latter method in selected areas has been found to be popular and entirely satisfactory.

As the committee was now satisfied that with regard to the extent of infection the county was not as bad as it was painted, it decided to adopt the quicker method

in subsequent visits, especially as it proposed to extend its activities to the rural parts of the county, where less infection would probably be found, while also finishing off the remaining urban schools. Over a period of four months four further batches of schoolchildren were tested. Propaganda in the Press and from the pulpit was instrumental in inducing people to bring their pre-school and "teenagers" (two extremely important groups from the point of view of anti-tuberculosis work) to swell the number of schoolchildren, and batches of 1,623, 1,080, 1,087, and 1,600 came for examination.

These different batches were completed in the course of four different weeks, as the county health officials had prepared the way during the week preceding the vaccinator's visit by giving the preliminary tests of Moro's ointment or 1/5000 O.T. So the vaccinator completed his work in each series of schools on Monday and Wednesday, Tuesday and Friday, and Thursday and Saturday. To save wearisome lists of statistics the whole six batches have been combined and are given in Table III.

TABLE III

	Moro Test		1/5000 O.T.		1/100 O.T.		Total Pos.	% Pos.
	No.	Pos.	No.	Pos.	No.	Pos.		
Urban ..	3,139	456	1,787	224	2,123	133	813+90	28·6
Rural ..	4,495	217	634	95	3,724	213	525+29	12·3

The whole six batches have been combined again to show the different percentages for the varying age groups, and are shown in Table IV, differentiating between urban and rural districts.

TABLE IV

Age	Urban			Rural		
	No. Tested	Pos.	%	No. Tested	Pos.	%
0–2	85	4	4·7	257	10	3·8
3–5	281	43	15·3	631	50	7·9
6–10	1,010	213	20·0	1,413	141	9·9
11–15	1,279	426	33·3	1,297	160	12·3
16–20	450	192	42·6	608	97	15·9
Over 20	34	25	73·5	289	96	33·2

The statistics in Table IV demonstrate the high degree of infection found in an urban area compared with that found in a rural area even when the urban area is not highly industrialized, and the higher infection rate can only be explained by the more intimate contact inevitably associated with a population living in great numbers in working-class districts and in tenement rooms. Both sets of figures also show that the amount of infection existing in Co. Sligo is no greater than in other areas and that the reputation of the county as a hotbed of tuberculosis is not justified. Some recent figures for infection in other areas are as follows. Ho'm (Public Health Report, September 6, 1946), in the Danish State Schools in 1942–5, found 14.7% of children infected at the age of 10, 37.7% at the age of 15, and 58% at the age of 20. Rich (1944) estimates that in the United States Registration area 10% are infected at 5 years, 25% at 10 years, 35% at 15 years, and 45% at 20 years. Pointon Dick (1950), with one test only, found 5% positive at 5–7 years, 14% at 8–10 years, 32% at 11–15 years, and 39% at 15–20 years. Scallan (1951), who was one of the hardest workers in our Sligo campaign for the past year, found 50% of the children infected in a town in another Irish county, as compared with 27% in Sligo town.

B.C.G. Vaccination

B.C.G. vaccination was carried out on 4,750 children and adults who proved negative to all tests; no casualty or accident occurred throughout, and beyond a few sore arms which healed in a very short time there were no complaints. That there were no such complaints or accidents is a proof of the efficiency of the organization and systematic control exercised by the National B.C.G. Committee, which gets regular supplies of the vaccine by air from Sweden every week, and has a very elaborate system of records for each person vaccinated, including data on all results, size of local reaction, amount of erythema, and induration in tuberculin reactions. As these records cover results from all Eire, the Committee is accumulating many valuable data which will be the basis of further research.

For some years past attention has been drawn in our Annual Report to the number of young adolescents returning home from England with established disease, and the opinion has been expressed that the chief cause of this was that they had gone into industrial life while still tuberculin-negative. Our findings during the present campaign go a long way to confirm this, and we have endeavoured, especially in the last few groups done, to persuade as many young adults as possible to be vaccinated before emigrating.

The National B.C.G. Committee has now taken over the entire work in the country and has sent its own team here; it is hoped that every parish in the county will have been visited and vaccination carried out within the next few months.

Discussion

The ultimate result of the vaccination campaign is of course a matter for the future, and benefits attributable to it will be apparent in our statistics only after the lapse of some years. We have complete lists of the children on the various school rolls, and those children who refused or who were absent from vaccination will serve as some sort of a control group to those who were vaccinated. At the cost of a considerable amount of work and trouble on the part of the committee and its officials all the vaccinated have been tested after the lapse of six to eight weeks (the post-vaccinal test) to ensure that the vaccination has been effective, and in cases of failure revaccination has been carried out. The value and importance of the post-vaccinal test cannot be overemphasized. In some cases it has been found that the vaccine has not taken, and in those cases revaccination is necessary. Those persons who have not returned for the post-vaccinal test may be living in a fool's paradise, believing themselves protected against the disease when in reality they can have no certainty of protection. Should they develop disease later the vaccination in their cases will be accounted a failure. In justice to B.C.G. vaccination and to the patients themselves the post-vaccinal test is essential. It is of course proposed to carry out yearly or two-yearly tests to estimate the duration of immunity and to ensure that any who revert to the negative tuberculin state will be given the benefit of revaccination.

Apart altogether from benefits that we believe will eventually be established from the widespread B.C.G.

vaccination, the tuberculin-testing survey has been found of very great interest, and we regard it as of very great help in our ordinary anti-tuberculosis work.

One impression formed during the year is that the tubercle bacillus is not so prevalent or ubiquitous as we had formerly supposed, that when it settles it "stays put," but that where it does "stay put" it invariably makes its presence known by positive reactors in its neighbourhood.

In some rural schools not one single reactor was found, and where schools showed more than an average percentage of positives open cases were present in the area or there was a very strong indication to us to seek the source in the immediate neighbourhood.

From our work during the year we have learnt that in future when we come across a positive reactor it will be our duty to try to trace the source, and, while this may be impossible in the towns, it should be possible in rural areas. We should not, as we formerly did, regard a positive reaction as the expected and universal result, but as an indication that the reactor got his tuberculin sensitivity from an open case of pulmonary tuberculosis; and, if we have no suspicion already about the source, that open case should be located. The younger the reactor the more restricted will be his environment and the more limited the search. In the continued campaign in this county in one week, out of 387 persons aged from 6 months to 35 years 34 reactors to the full series of tests were found. This of course was in a rural area. There has not been time to study this series properly, but for the purposes of this paper a hasty analysis of the data from their record sheets has been made, with some interesting results. Of the 34 reactors three are contacts to already known cases, and nine, all of them with the exception of one 8-year-old over 10 years of age, are isolated cases—that is, one case to each household. In the latter cases there would be very little possibility of tracing the source of infection. The remaining 22 cases are grouped in a significant manner: There are two homes with three reactors and eight homes with two. The age incidence of some of those groups are: 2½ and 3½; 3.7 and 9; 10.6, 13.6, and 16; 7 and 9 years. It is felt that thorough investigation in those homes would be well worth while. Those children have either obtained their sensitivity from an open case in their immediate neighbourhood or they are victims of a bovine infection. In either instance the discovery of the source of the infection should not be impossible in some of these cases. Because of the number of persons over 50 (three of them between 65 and 70) diagnosed as open cases in the last few years, particular attention will be paid to the old bronchitics and chronic coughers who are so common in rural areas. Filming and sputum examination in those cases will, it is thought, pay higher dividends than the mere *x*-raying of reactors. This was tried fairly extensively last year, with the result that very little treatment was indicated except in the case of very young children. We expect a visit soon from a mass radiology unit, and this should complete a rounded campaign.

It should be said in conclusion that the opinions and impressions noted in this article are personal to me, and are not necessarily shared by the National B.C.G. Committee or its medical personnel.

The grateful thanks of the County Public Health Department are due to the National B.C.G. Committee, St. Ultan's Hospital, Dublin, and their officials, Dr. J. St. P. Cowell, Medical Director, Dr. P. Alston, and Dr. B. Scallan, who of course are responsible for all the work detailed above, the writer acting merely as organizer and enthusiastic supporter. Thanks are also due to Dr. Michael Kirby, County Medical Officer of Health, for permission to publish this article, to Dr. Kirby and Dr. Cowell for generous co-operation in compiling it, and to our nursing and clerical staff, on whom the heavy work of the whole county campaign fell.

ADDENDUM.—Since the preparation of this paper the committee has completed its programme for the county, and its members have visited every district and school. In all, 11,786 children under 15 years of age have been tested. Of these, 10.9% were positive, and 8,735 were vaccinated. 2,616 persons over 15 years old were tested. Of these, 28.9% were positive and 1,364 were vaccinated. A small portion of those vaccinated have not yet had a post-vaccinal test, but of those who have had it 95% were positive after the six-weeks or eight-weeks interval: these of course were revaccinated. For the purposes of this paper a small number of cases (140) vaccinated in March, 1950, were tested after 15 months' interval, and 97% of these were still positive. A complete list of all positive reactors in the different dispensary areas has been circulated to the medical officers concerned, and especial attention drawn to households with two or more cases. This knowledge should prove of great value to the doctor in future dealings with his district.

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CONGENITAL DUPLICATIONS OF THE SMALL INTESTINE

BY

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Duplications of the small intestine are uncommon, and may be of spherical or tubular shape. The spherical cyst must be distinguished from a Meckel's diverticulum, which is due to the persistence of the vitelline duct, and from other minute diverticula. These arise from the epithelium lining the intestine, and grow into the subepithelial connective tissue, and come to lie principally on the antimesenteric side of the intestine. The spherical duplication cysts are situated between the layers of the mesentery, on the mesenteric side of the intestine. These cysts must also be distinguished from the thin-walled mesenteric cysts of lymphangiomatous origin, whereas the duplication cysts have thick walls containing all layers of the small intestine. The former can be separated easily from the small intestine, and the latter only with difficulty.

Summaries of recorded cases have been made by Normark (1937), and by Bremer (1944), and Ladd and Gross (1940) described a series of 18 personal cases. Recently Wooller (1950) described one case of the cystic type, and Aitken (1950) recorded a very rare case of duplication of the intestine from a Meckel's diverticulum to the anal canal.

Two cases of this condition have been operated upon in the Leicester Royal Infirmary in the last five years, one being of the tubular type, and one of both cystic and tubular type. Dr. E. M. Ward, the senior pathologist,

has also noted one case of the tubular condition found at the post-mortem examination of a child who died from tuberculous meningitis.

Case 1

A female infant aged 5 months was admitted to hospital on October 2, 1949, under Dr. J. C. V. Braithwaite, whose diagnosis was "haemorrhage from a gastric ulcer of a Meckel's diverticulum." The child had always been well, but that evening she passed a fair amount of bright-red blood about 8.30 and thereafter cried a lot. The bowels were not open at this time.

On admission she appeared to be a well-nourished baby, and was apparently contented, although definitely anaemic. No abnormality could be found on abdominal or rectal examination, but a small quantity of dark blood followed withdrawal of the finger. There was no mucus. On October 3 there was further rectal haemorrhage, with some bright blood in a black stool. The haemoglobin was 47%. A whole-blood transfusion of 120 ml. was given into the external jugular vein. Next day the haemoglobin was 57%. Melaena occurred on two occasions on the 5th. The case was referred to me on October 6 with a view to surgical treatment. Sigmoidoscopy on the 7th revealed nothing abnormal in the lower 5 in. (12.5 cm.) of the bowel. Further melaena occurred on the 8th, and on the 10th the haemoglobin was 64%. A further transfusion of packed cells (130 ml.) was given into a scalp vein on October 13. At operation on October 14 the small intestine was found to be duplicated in the lower ileum at a point 6 in. (15 cm.) from the ileo-caecal valve. The duplication extended proximally for about 8 in. (20 cm.), where it ended in a blind pouch; 1½ in. (3.75 cm.) from the point at which the duplication joined the normal intestine there was a hard ulcer-like mass. The bowel was resected and the lumen restored by an end-to-end anastomosis.

Post-operative progress was uneventful, the bowels being open normally on October 17. The child made a complete recovery, and *x*-ray examination of the chest showed no abnormality.

Pathology (Dr. E. M. Ward).—"The specimen consists of a loop of small intestine, on the mesenteric attachment of which there is a second loop approximately 7 in. (17.5 cm.) long, and with a similar diameter. There is an opening into this internal loop ¼ in. (0.6 cm.) in diameter. On dissection of the internal loop it is seen that the mucosa has the macroscopic appearance of gastric mucosa; 1½ in. (3.75 cm.) from the point where this loop joins the main portion of bowel there is a subacute ulcer which almost perforates into the main bowel."

Histology.—"Examination confirms that the lining of the second loop is gastric mucosa, and the ulcer is shown as a typical subacute peptic ulcer."

Case 2

A female infant aged 3 weeks was admitted to hospital on June 22, 1944, under Dr. J. C. V. Braithwaite, with a history of vomiting since leaving the nursing-home, the date of which was not given, although it was presumably 14 days after birth. The bowels had been open daily. The child was a full-term first baby, the birth weight being 8 lb. 6 oz. (3.8 kg.). The abdomen was distended, with violent visible peristalsis, associated with screaming and drawing up of the legs. A firm swelling was palpable on the left side of the abdomen, apparently coming from the left loin. Hb was 98%. The pre-operative diagnosis was a polycystic kidney or mesenteric cyst.

Operation.—On June 27 Mr. E. R. Frizelle operated through a right paramedian incision. Collapsed small intestine presented in the wound on opening the peritoneum, and there was a cystic swelling to the left of the midline. The cyst was aspirated and delivered to the surface, being followed by distended small intestine. The cyst, which was 4 in. (10 cm.) in diameter, was in the mesentery of the small intestine about half-way down the ileum. It was close to the bowel wall at one point, but no definite attachment was demonstrated. The vessels to the adjacent ileum coursed over the cyst. There were two areas of reduplication of the small intestine, one above and one below the cyst. The upper reduplicated area was 18 in. (45 cm.) in length. The accessory portion was dilated, but had no connexion with the ileum. There was a similar accessory dilated portion of the terminal ileum 18 in. in length running along a collapsed ileum up to the caecum, and at one point the finger could be passed between the distended and collapsed adjacent coils. This distended portion was anastomosed to the caecum in one layer. There was a small-bowel obstruction due to the intestine having been twisted by the cyst. This twist was relieved. A tube was inserted into the cyst, which was fixed to the anterior abdominal wall by a catgut stitch. The wound was closed in layers around this tube.

The child made a slow recovery, and was discharged from hospital with normal bowel function on July 28. She was, however, readmitted shortly afterwards, and died on August 4 from apparently acute intestinal obstruction. The post-mortem record of this case is unfortunately not available.

Case 3

This patient was a boy aged 2½ years. Necropsy was carried out on October 11, 1949, by Dr. E. M. Ward, who reported as follows. "The brain shows typical tuberculous meningitis, together with vascular stasis. There are no intracerebral tubercles." A primary focus was present in the lower lobe of the right lung, with associated tuberculous lymph nodes in the hilum of the lung and at the bifurcation of the trachea. Abdomen: situated about 3 ft. (91 cm.) from the ileo-caecal junction is a portion of double small bowel, 6 in. (15 cm.) in length. The second loop is attached to the mesenteric border of the ileum and opens into normal bowel at the lower end. There is no evidence of secretory retention or of inflammation."

Discussion

These conditions have been very fully described by Ladd and Gross (1940), who group the cystic lesions which may occur along various points of the alimentary canal under the heading of "duplications of the alimentary tract" (enterogenous cysts, enteric cysts, or ileum duplex). Their suggestion regarding the aetiology is "that they are primarily produced by pinching off a small bud from the gut wall, with development of the segregated tissue into a cystic structure adjacent to the normal intestine."

Bremer (1944) reviewed the literature. He considered that the group of anomalies comprising enterogenous cysts, intestinal duplications, and the like is divisible into two smaller classes on the basis of embryological origin.

Normark (1937) emphasizes the association of enterogenous cysts of the chest in these cases of congenital duplication of the small intestine. The mucosal heterotopia in these cases has not been satisfactorily explained.

Clinical Features.—The cases described above well illustrate the different manner in which these cases may present. Case 1 showed the type with melaena or severe rectal haemorrhage in an infant or young child. Case 2 showed the more severe type, presenting with symptoms and signs of intestinal obstruction. This case also illustrates the multiplicity of lesions that may be present and the extreme difficulty of treatment in such a case. Case 3, so far as is known, had shown no evidence of the condition up to the time of death from a second pathological condition. In Case 1 there was no radiological evidence of an enterogenous cyst of the chest, and no such cyst was found at necropsy in Case 3.

Summary

Three further cases of congenital duplication of the small intestine are recorded, and attention is drawn to the association of the condition with enterogenous cysts of the chest.

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Medical Memoranda

Restoration of Speech in Severe Aphasia by Intravenous and Oral Priscol

The following case is of interest because of the temporary but extraordinary efficacy of "priscol" (tolazoline), and because, although many papers have emphasized the value of priscol in peripheral vascular states, none has been concerned with the effect of the drug on the cerebrovascular system.

Case Report

A man aged 55 was admitted to Barrow Hospital in November, 1950, in a state of agitation. Depressive episodes had occurred before and had necessitated at least four periods in various hospitals and nursing-homes. Together with the agitation and depression he showed a mixed type of aphasia, mainly motor, with almost complete agraphia. He was unable to find words to express his needs, although by gesture he usually made himself understood. He was also able to respond by actions to commands, whether given verbally or in writing. There was no clouding of consciousness. Perseveration in speech was marked, and it was quite clear that the inability to write his requirements occasioned him great upset, and after a few attempts he usually lay back in bed, the picture of tearful misery and distress.

He was of athletic habitus, with good nutrition, showing marked peripheral arteriosclerosis and a retinopathy of about Grade II significance (Wagner and Keith). Serial blood-pressure readings showed a mean of 150/95.

On investigation the urine was normal, and the W.R. and Kahn tests were negative. Radiographs showed that the heart was slightly enlarged in its transverse diameter, and that there was considerable calcification of cerebral vessels. Electrocardiograms revealed left axis deviation only. A blood count showed: Hb, 12.5 g. (80% Sahli); red cells, 4,210,000 per c.mm.; white cells, 10,400 per c.mm. (differential count normal). Electroencephalograms did not reveal any focal signs. Lumbar puncture showed a pressure of 180 c.mm. H_2O; no ventricular or spinal block. The fluid was clear and colourless, with 1 lymphocyte per c.mm. Globulin was normal; protein, 40 mg. per 100 ml. Lange, normal. W.R. negative.

Psychological examination showed that he was probably a man of superior previous intelligence, with learning and memory failure; the perseverative quality and complete failure to improve suggested an organic origin.

Because of the above symptoms, signs, and investigation results, he was regarded as a case of organic brain change with aphasia due to cerebral arteriosclerosis, but with no evidence of a focal lesion.

Treatment

The above state continued for three weeks with some fluctuations. Occasionally his speech improved, and the nominal difficulties and perseveration tended to lessen for a few hours at a time, but never completely disappeared, while the inability to write persisted throughout.

As a result of these fluctuations in the clinical state and a consideration of the underlying pathology, which was believed to be one of arteriosclerosis, an attempt was made to improve the cerebral circulation by opening up collateral arterioles. Accordingly he was given a test intravenous injection of 40 mg. of priscol, very slowly. Two minutes later his face and conjunctivae became very flushed, and the retinal vessels were noted to be wider than before. Serial blood-pressure readings indicated a rise in the systolic but a definite fall in the diastolic pressure (systolic 150–158, diastolic 95–75 mm.). The pulse rate increased from 74 to 96 over the next seven minutes. Together with these physiological changes there was a most remarkable improvement in his speech. Exactly four minutes after the injection he sat up in bed, saying he felt "wonderful," and it was clear that he could find words to express anything. Moreover, for the first time he was able to write his name and to copy sentences. His emotional disturbance disappeared, and he was in every way considerably improved. This effect lasted about three hours, but afterwards he rapidly returned to his aphasic condition and his previous state of agitation.

The above procedure was tried again, with exactly the same results, and a record was made on the magnetic tape recorder, which allowed the great differences in the speech performance to be noted.

To evaluate the effect of suggestion, first normal saline and later vitamin B_1 were given intravenously with exactly the same preparations and precautions as used in the priscol experiment, but there were no results whatsoever. Nicotinic acid was also used, and certainly produced the physiological effects of a peripheral vasodilator, but brought no improvement in his speech function. During one of the "lucid intervals" after a priscol injection, psychological testing showed a good performance on learning tests and no evidence of memory failure.

It was decided to treat him regularly with oral priscol, and he was given 25 mg. six times a day. After 48 hours his speech and his writing began to improve, and at the end of a week were practically normal. The distress and agitation were very much lessened, and it was quite clear that most of his emotional upset was due to his inability to speak.

About a fortnight later the tablets of priscol were stopped and a vitamin C preparation was given in its place, both tablets being identical in size and shape. At the end of the fourth day he showed deterioration, the difficulty in finding names becoming again very obvious.

A further intravenous injection of priscol rapidly resolved the aphasia, but as 75 mg. was required it was considered that he was becoming tolerant to the drug. Future events confirmed this hypothesis, as in spite of increased dosage (up to nine tablets a day) he slowly returned to his former state of motor aphasia and agraphia and his depressed and agitated condition.

Comment

Although the results of this case were ultimately poor, it is felt that similar therapeutic trials would be of value, especially in cerebral arteriosclerotics with minimal intellectual failure, in some of whom it may have a more lasting effect.

It is probable that priscol could act in only one of two ways in this case: either by means of its histamine-like action on arterioles, causing increased dilatation in the affected area and in the region surrounding it, so that more oxygen might be available in the area of depressed function; or, assuming the arterioles to be affected by arteriosclerotic changes but still partly capable of spasm, by its physiological effects actually relieving this spasm. The latter is less probable, as both lack of oxygen and excess of metabolites—especially CO_2, as can be expected in a relatively ischaemic area—are potent vasodilators, making any spasm improbable.

Another interesting fact in this case is the rapidity of response after such a considerable period of aphasia, indicating that the cerebral structures involved were functionally depressed and not destroyed. The immediate change in the psychiatric picture after the return of the speech function was especially striking and very instructive.

We would like to thank Dr. R. E. Hemphill for advice and permission to publish this article.

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An Unusual Case of Hypoprothrombinaemia Haemorrhagica

Haemorrhagic states associated with hypoprothrombinaemia are well known to occur clinically in two sets of conditions—in the neonatal period and in liver diseases with obstructive jaundice. The case reported here, however, falls in neither category, and is presented because of its unusual features.

Case Report

The patient, a woman aged 50, complained of tenderness of the extremities along with the appearance of "reddish patches" of varying sizes and distribution in the limbs and trunk. She had been apparently well until early the previous evening, and had not noticed any pinkish areas on her body or experienced any discomfort. She was definite that all her symptoms developed in the course of a few hours, late the previous evening and overnight. Patches were appearing continuously and increasing in size. The most careful questioning failed to reveal any allergic basis whatsoever for these symptoms. There was no history of bleeding from any of the orifices. Her periods had stopped four years ago. She was sure that there was nothing unusual about her diet or surroundings which could have caused these symptoms, and she had not taken any drugs or unusual foods.

An exactly similar attack ten years ago was characterized by the rather abrupt occurrence of pinkish patches over her extremities and trunk. The patches lasted then for a few days, gradually turned dusky, and disappeared under some treatment the details of which were not available.

On examination the patient seemed obviously ill but not toxic, and was unable to walk or move about normally

Fig. 1.—Condition before treatment.

because of the tenderness in her limbs. Her temperature was normal. There was evidence of extensive subcutaneous haemorrhage in the extremities and trunk. The lateral aspects of both thighs presented large pinkish areas of subcutaneous haemorrhage (Fig. 1). The rest of the limbs and trunk showed haemorrhagic patches of varying sizes ranging from punctate spots to large patches. The largest was an oval-shaped patch in the right thigh measuring 6 by 3 in. (15 by 7.5 cm.). The trunk showed fairly extensive areas of subcutaneous haemorrhage, particularly in the lower back. The upper limbs were less heavily involved. The face was exempt; the tongue and buccal mucous membrane were normal. These pinkish patches were not elevated above the skin surface and were not itchy.

Active movements of the extremities were painful, and vigorous passive movements were also resented. The joints were not swollen or particularly tender; the heart and lungs were normal; the blood pressure was 100/70 mm. Hg; no abnormality of the central nervous system was detected; the liver and spleen were not palpable; and examination of the abdomen revealed no abnormality.

Haematological examination showed: red cells, 4,300,000 per c.mm.; Hb, 10.6 g.%; P.C.V., 34%; M.C.V., 80.4 μ^3; M.C.H., 25.1 $\mu\mu$g.; M.C.H.C., 31%; white cells, 7,200 per c.mm.; platelets, 235,000 per c.mm.; prothrombin time, 125 seconds (Quick's method). The bleeding and clotting times were normal. Fractional gastric analysis showed nothing unusual. Examination of the urine and stools revealed nothing abnormal.

Fig. 2.—After treatment.

Because of the marked increase in the prothrombin time vitamin K was tried, 10 mg. of vitamin K (2-methyl-1,4-naphthohydroquinone; "synkavit") being injected intramuscularly daily for the first four days and on the sixth and seventh days. Once the treatment was started no fresh areas of bleeding were noticed. Gradually the pinkish areas turned dusky and began to fade, and by the fifth day no trace of them was left (Fig. 2). The tenderness of the limbs also rapidly disappeared.

The prothrombin time showed a progressive decline from 125 seconds before treatment to 50 seconds on the third day of treatment, 18 seconds on the fifth day, and 15 seconds on the seventh day.

A follow-up of the patient shows that she is keeping in good health.

Comment

The occurrence of hypoprothrombinaemia haemorrhagica in the neonatal period and in obstructive jaundice is well recognized and explained. In the case reported here, however, haemorrhagic manifestations associated with hypoprothrombinaemia were seen in an adult not suffering from any liver disorder. There is apparently no explanation for the hypoprothrombinaemia in this case. The diet was apparently adequate and there was no intestinal upset. Kallos (1946) has reported beneficial results from treatment with vitamin K in cases of angioneurotic oedema without allergic bases but associated with hypoprothrombinaemia. We are not aware of any reports of purpuric manifestations associated with hypoprothrombinaemia in adults not suffering from liver disorders.

We are grateful to Messrs. Hoffmann-LaRoche for the free supply of synkavit.

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Reviews

TRANSMISSION OF NERVE IMPULSES

The Transmission of Nerve Impulses at Neuroeffector Junctions and Peripheral Synapses. By Arturo Rosenblueth. (Pp. 325; 98 figures. £2 8s.) New York: Published jointly by the Technology Press of Massachusetts Institute of Technology and John Wiley and Sons, Inc. London: Chapman and Hall.

Professor Rosenblueth, now professor of physiology and pharmacology at Mexico City, had earlier shared responsibility with the late Professor W. B. Cannon for two important and attractive monographs from the Harvard Laboratory dealing with the same field of research as the volume under review. Neither of these earlier books had aimed, as some monographs do, at a merely impartial and colourless compilation of the evidence from all sources They had, on the contrary, something of the personal, narrative character which gave an unusual interest and charm to so much of what Cannon wrote, even for specialist readers. Such a method obviously lends itself better to the advocacy of individual interpretations and theories than to a strictly judicial summary.

The same method is adopted by Professor Rosenblueth in this new publication of what is, essentially, a recasting and extension, to meet recent advances of the subject, of the earlier book with Cannon on *Autonomic Effector Systems;* and some may think that this personal note, in the presentation of a subject with which the work of so many laboratories and experimenters has been concerned, has here been sounded rather insistently. A quick survey of the many illustrations, for example, might give the impression that the investigations of the author and his co-workers have played even a predominant part in creating the basis for the newer developments, especially those concerned with transmission at peripheral synapses (Part 2). A glance at the admirably complete and most welcome reference-list and indexes might give a similar impression. The author-index, for example, shows that Professor Rosenblueth's published observations and ideas are cited 175 times in the text, while those of his late teacher, Professor Cannon, and of Professor Eccles, have each to be content with scores in the 50's, and no other worker in the field reaches 40. Professor Rosenblueth has undoubtedly made valuable contributions to the subject, but hardly, one may suspect, of a significance to justify that proportion, on an impersonal scale of comparison. Nevertheless, it is very useful to have access, in one handy volume, to all that he has done and thought in this direction; and of special value, perhaps, is the collection here of all his observations on the electrical responses of smooth muscle.

One considerable section of the book appears to me to be, frankly, disappointing. There were certain now familiar discrepancies in detail between the actions of adrenaline on the one hand and those, on the other hand, of sympathetic nerve impulses and, as Cannon and Rosenblueth so abundantly emphasized, of the sympathetic transmitter "sympathin," as it escapes naturally into the circulation. Cannon and Rosenblueth had elaborated their well-known theory of the two sympathin-complexes, E and I, essentially to explain these discrepancies. On the other hand, it had seemed clear for many years to some, myself among them, that these discrepancies might find a much simpler explanation, if there were evidence of the presence in the body and appropriate distribution in the sympathetic system, in relation to that of adrenaline, of the primary amine, *nor*-adrenaline; the main lines of the differences in detail between the actions of these two amines having been known since 1910. Now, in the past few years, the evidence has poured in from many sides, showing that *nor*-adrenaline is present in the body, having a general predominance over adrenaline in its distribution in adrenergic nerves and in the transmitter as directly collected, and to just the degree required to explain these long-known discrepancies. Yet, instead of sharing a general relief from any further need for a complicated theoretical expedient, Professor Rosenblueth devotes two whole chapters (3 and 4), of some 27 pages in all, to discounting the significance of this new evidence, and insisting, in spite of it, on the still unimpaired validity of the theory of the two sympathin-complexes. He admits, indeed, that, "if one of these mediators (i.e., *nor*-adrenaline and adrenaline) were exclusively or primarily excitatory and the other primarily inhibitory, the hypothesis of the specific receptive substances (i.e., E and I) would become unnecessary. *Nor*-adrenaline," he continues, "is mainly excitatory in its action, but adrenaline is not mainly inhibitory." Surely this is muddled thinking. "Mainly inhibitory" can only mean, I think, inhibitory of the activities of most of the effectors on which it acts at all; and I believe that it is the E and I theory, and not any experimental evidence so far available, which requires a sympathetic transmitter of such mainly inhibitory action. Do we, or does Professor Rosenblueth, demand of the acetylcholine liberated by impulses in the heart vagus that its action on all effectors should be "mainly inhibitory"? I am left puzzled by such loyalty to what seems to me a no longer necessary theory.

In many ways the book will be invaluable to explorers in the same direction as a book of reference and as a record of the procedures and the ways of thinking of an important, resourceful, and unwearying experimenter in this field. In arrangement and clearness of presentation it is admirable; but I feel that its personal character must diminish its value as a guide for those who have no special knowledge of its subject.

H. H. Dale.

HAEMOSTASIS

The Physiology and Pathology of Hemostasis. By Professor Armand J. Quick, Ph.D., M.D. (Pp. 188; 18 illustrations. £1 8s.) London: Henry Kimpton. 1951.

A previous book by Quick on the haemorrhagic diseases and the physiology of haemostasis appeared in 1942, but there have been so many developments that he has now written a new book. Quick has shown a flair for seizing hold of the important points in the difficult subject of blood-clotting, and the present book is a good example of his gift for clear exposition. The main change in the last decade has been to consider blood coagulation as a chain reaction, or rather a series of such reactions. The most important of them is the thrombinogenic cycle, which is normally controlled by the ability of the fibrin network to absorb thrombin so effectively that little is left to act on the platelets and start the cycle again. Out of this there has developed a conception of venous thrombosis in which emphasis is placed on the importance of clot retraction. Measurements of prothrombin consumption and of thrombo-

plastinogen have moved from the research laboratory into the hands of the clinical haematologist.

This book has five chapters on the historical background, the present theory of coagulation of the blood, the classification, diagnosis, and treatment of the haemorrhagic diseases, and venous thrombosis. In the second half of the book the author describes laboratory methods in complete detail. This section will be of immense value to other workers. The book as a whole can be strongly recommended as an up-to-date account, by an author who is not afraid to be dogmatic, of a subject which extends far beyond the confines of haematology and concerns all those who have to deal with vascular lesions and accidents.

L. J. Witts.

CANCER AND ITS TREATMENT

Cancer. Where We Stand. By Sidney Russ, C.B.E., D.Sc., F.Inst.P. Foreword by Lord Horder, G.C.V.O., M.D., F.R.C.P. (Pp. 192; illustrated. 10s. 6d.) London: Geoffrey Cumberlege (Oxford University Press). 1950.

The last fifty years have seen the development of a wide interest in cancer, and a book in simple language by so eminent an expert as Professor Russ is very welcome. The fact that he is a physicist and not a practitioner of medicine is in some ways an advantage, for it puts him in more intimate contact with the layman, for whom he chiefly writes. He explains in familiar terms all that is known about the incidence of the disease, the immense importance of its early diagnosis, and the prospects of permanent cure, which have been so greatly enhanced by modern methods.

The medical man will welcome reliable statistics from many sources, comparing the results of surgery and radiation and estimating their relative value in different fields. He will also appreciate a brief but accurate description of the physical nature of radiation and of the methods and precautions to be adopted in its use. Although everyone agrees that such powerful tools should be handled only by experts, it is of the greatest importance that every doctor should understand their powers and their limitations.

It is equally important that he should be able to convince his patients that cancer is not infectious, that in general it is not hereditary, and that if only recognized early there is a reasonable prospect of cure. He will find here all the information he can require to remove what is often a real anxiety and to replace it by a substantial confidence.

Henry Souttar.

PSYCHO-ANALYSIS OF CHILDREN

The Psychoanalytic Study of the Child. Volume III–IV, (Pp. 493. £1 15s.) Volume V. (Pp. 410. £1 15s.) Edited by A. Freud, W. Hoffer, and E. Glover. London: Imago Publishing Company. 1949.

Delay in reviewing the combined Vols. III–IV has put the reviewer in the humiliating position of being overtaken by Vol. V. His difficulties are thereby increased, since the trouble with these volumes is the quantity of the material they contain. They are indeed a kind of journal appearing in book form, and it is to be hoped that they will continue to appear yearly.

To read all that these two volumes contain would be a big experience for anyone to whom the subject has meaning, and the task of sorting out the very good from the mediocre a heavy one. In any case this task belongs to the more specialist journals. Here it is perhaps sufficient to remind those who are interested in child psychiatry and in the roots of mental health and mental disorder that these volumes contain important contributions to every aspect of dynamic psychology and its practice. Most happily, it can be reported that there is less "in-breeding" in the articles and references than in the first two volumes. Hitherto the contributions have come largely from one half of the psycho-analytic grouping—that which seems to the other half to edge away from the child's ideas of the inside of the psychosoma—but there is good reason why there should exist a place for publication of all kinds of sincere work.

The really valuable articles are too numerous in these volumes even to be listed here, but they include (Vol. III–IV) Anna Freud's contribution to a symposium on aggression, and an article by the late August Aichhorn, pioneer in the study and management of delinquents, on female juvenile delinquents. There is also an article in each volume by René A. Spitz, who is widely known through his observations, which appeared in Vol. II, on infants deprived of natural human relationships. These volumes provide, incidentally, a valuable link between psycho-analysis in the U.S.A. and psycho-analysis in Great Britain and Holland, and indicate the extent of the circle of friendships that has near its centre the personality of Miss Anna Freud.

D. W. Winnicott.

SOME GLASGOW PIONEERS

An Eighteenth Century Lectureship in Chemistry. Essays and Bicentenary Addresses relating to the Chemistry Department (1747) of Glasgow University (1451). Edited by Andrew Kent, M.A., Ph.D. With foreword by J. W. Cook, F.R.S. Glasgow University Publication No. LXXXII. (Pp. 233; illustrated. £1 1s.) Glasgow: Jackson, Son and Co. 1950.

In 1747 the University of Glasgow established within its Faculty of Medicine a lectureship in chemistry. The first two holders were William Cullen and Joseph Black. These two—medical men, like four of the five lecturers who succeeded them—were pioneers of science and of education. Their achievements, the academic and industrial background of their time, and the later evolution of the Chemistry Department which they founded and fostered in Glasgow were the subjects of four bicentenary addresses delivered in 1947 by Dr. Douglas Guthrie, Professor John Read, Dr. Alexander Fleck, and Professor A. R. Todd. Under the competent editorship of Dr. Andrew Kent the substance of these addresses and authoritative supplementary essays by many distinguished contributors have now been assembled into a book of compelling interest and historical value.

Although chemistry in Glasgow is the acknowledged and recurrent theme, neither the city nor the subject is allowed to confine a proper appreciation of scientific events and their consequences. Indeed, had the writers set out to show that science is a whole and its adherents a variety of men, they could scarcely have succeeded better. But this feature of the book is perhaps less the result of concerted purpose than the true reflection of an age when the engineering genius of Watt found its stimulus in the work and conversation of his medico-chemical associates, Black and Robison. Breadth of interest, quickened by discussion and the impact of strong personalities, was characteristic of the period, and it is well maintained in the book.

The seven incumbents of the lectureship are presented in pen-pictures, drawn with understanding of the contemporary scene and supported by the reproduction of portraits—four of them by Raeburn. The influence they exerted both at home and abroad—in science, medicine, and industry—is closely followed and discussed, and there emerges from this collection of articles a well-co-ordinated, fully documented book which makes a real contribution to the history of science and of medicine.

JAMES D. LOUDON.

THE ETHER CONTROVERSY

The First Anesthetic. The Story of Crawford Long. By Frank Kells Boland, M.D. (Pp. 160; illustrated. $3.) Athens: University of Georgia Press. 1950.

The story of the discovery of surgical anaesthesia in the U.S.A. is well known in Britain, and many are familiar with the fact that the belated claims made by Crawford Williamson Long, of Georgia, led to some feeling in the South that their hero had not been given due credit for his part in the discovery. The author of this book is president of the Crawford W. Long Memorial Association. In the publisher's announcement on the dust-cover we are advised that Dr. Boland "has continued his studies and researches with the determination to establish Crawford Long as the real discoverer of anaesthesia." This is not an encouraging introduction to the book. History is not written in that way, and the statement makes the author's work suspect. On p. 106 Dr. Boland says: "We may be going out of the way slightly to build up Dr. Jackson's chances of deceit, but the case calls for imagination to match his methods. . . . The whole motive is to present Long as the discoverer, the originator, of surgical anaesthesia; Jackson as the messenger to Morton; and Morton as the public demonstrator of medicine's greatest gift to humanity."

The main facts are so well known as scarcely to merit repetition here. In 1840 Long, then aged 25, set up in practice in Jefferson, Georgia, and in December, 1841, or January, 1842, he introduced sulphuric ether to the young men of the town for the purpose of giving them amusing entertainment—as a substitute for the nitrous oxide used at such parties. On March 30, 1842, he used ether as an anaesthetic for the removal of a superficial tumour from the neck of a young man named James Venable. Three months later he removed a second tumour under ether from the neck of Venable. By October, 1846—the month in which Morton gave his famous demonstration in Boston—Long had performed eight operations, none of a major character, under ether anaesthesia, and after that date he performed at least twenty-one similar operations. But, although Long made no secret of what he had done, he did not publish his cases until 1849, by which time surgical anaesthesia was in use all over the world. Morton gave his demonstration at the Massachusetts General Hospital on October 16, 1846. At the end of the previous month he had discussed the question of anaesthesia with C. T. Jackson, a noted geologist, who was also notorious for his attempts to steal the inventions of others. In the "ether controversy" which later resulted it was never very clearly established whether at this interview Jackson had actually advised Morton to try ether. In any case, Morton had certainly been experimenting with ether, but had not so far performed an operation on a patient under its influence.

Dr. Boland sets out to show that the ubiquitous Jackson had, at some time between 1842 and 1846, been in Georgia and had there heard about Long's use of ether. That being accepted, he also asks us to accept the fact that Long—despite his own admitted failure to publish any of his cases—was directly responsible for Jackson's suggesting ether to Morton, and hence to the establishment of ether anaesthesia in both hemispheres. Unfortunately for his case, he produces no shred of evidence that Jackson had ever heard of Long or his work.

The introductory chapters of this book do not on the whole indicate a sound and comprehensive knowledge of the history of anaesthesia. Many of the sources quoted are second-hand; and although an imposing bibliography, containing many first-class works, is appended, Dr. Boland does not show real familiarity with these books. There are a number of minor errors—including the caption "William H. Morton" below the portrait of W. T. G. Morton. While this book adds accounts of a number of interesting events in the life of C. W. Long, it does not fundamentally alter the accepted position: Long was the first to give ether by inhalation for a surgical operation, but he had no place in introducing ether anaesthesia to the world.

E. A. UNDERWOOD

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

The History of Pharmacy. Catalogue of an exhibition held during the Festival period May 4 to September 28, 1951, at the Wellcome Research Institution. (Pp. 59. 3s.) London: Geoffrey Cumberlege. 1951.

The Organization of Bones. By Professor P. Lacroix. Translated by S. Gilder, B.Sc., M.B. (Pp. 235. 25s.) London: J. and A. Churchill. 1951.

Diseases of the Fundus Oculi. With Atlas. By Professor A. Fuchs, M.D. (Pp. 381. 112s. 6d.) London: H. K. Lewis. 1951.

The Anatomy of the Gorilla. Edited by W. K. Gregory. (Pp. 259. 97s. 6d.) London: Geoffrey Cumberlege. 1951.

A Field Surgery Pocket Book (Revised). Memoranda mainly based on experience in the 1939-45 war. Prepared under the direction of the Director-General of Army Medical Services. (Pp. 187. 4s.) London: H.M.S.O. 1950.

The Individual and His Religion. By Professor G. W. Allport. (Pp. 163. 12s. 6d.) London: Constable. 1951.

Modern Treatment Year Book 1951. Edited by Sir Cecil Wakeley, K.B.E., C.B., M.Ch., D.Sc., P.R.C.S., F.R.S.Ed., F.A.C.S., F.R.A.C.S. (Pp. 360. 17s 6d.) London: Baillière, Tindall and Cox. 1951.

Royal College of Surgeons of England: A Record of the Years from 1901 to 1950. Edited by E. Finch, F.R.C.S. (Pp. 79. 5s. paper cover; 8s. 6d. bound.) London: Royal College of Surgeons of England. 1951.

The Normal Encephalogram. By L. M. Davidoff, M.D., and C. G. Dyke, M.D. 3rd revised ed. (Pp. 240. 42s.) London: Henry Kimpton. 1951.

The Manchester School of Obstetrics and Gynaecology. By J. W. Bride, M.D., B.S., Ch.B., F.R.C.O.G. (Pp. 26. 3s. 6d.) Manchester: John Sherratt. 1951.

Cost Accounting for the Pharmaceutical Industry. Report of the Costing Committee appointed by the Council of the Association of British Pharmaceutical Industry. (Pp. 109. 25s.) London: The Association of British Pharmaceutical Industry. 1951.

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OUR DAILY BREAD

A hundred years ago the practice of the adulteration of food had assumed such proportions that a campaign of publicity against the purveyors of falsely described and poisonous preparations opened by the *Lancet* was followed by a series of Acts of Parliament. These were designed to support the efforts of a few enlightened public analysts and medical men, and, as a result, the practices of criminal adulteration were virtually stamped out. To celebrate this centenary a symposium was organized by the Nutrition Society last March, and an interesting comparison was drawn between the conditions to-day and those of 100 years ago. There is, for instance, still great anxiety about the quality and purity of the food sold to the public: in a recent discussion on the subject in the House of Lords[1] the carefully balanced reply of the Government spokesman stood in contrast to some of the wilder statements made by earlier speakers, whose remarks served, however, to illustrate the dangers, understandable enough, of losing a sense of proportion in arguments about the purity of the nation's food supply. A more sober and comprehensive discussion was recently held by the Society of Chemical Industry (reported on page 905).

No living organism from bacteria to *Homo sapiens* can flourish or function unless it is provided with a properly balanced supply of nutrients. A great many of the facts about the influence of agricultural, processing, and manufacturing practices on the quality of our food are marshalled by Sir Edward Mellanby in the opening pages of this issue. Having discussed some of the methods which lead to the introduction of foreign chemicals or changes in the nature of some of the ingredients of food, Sir Edward suggests that some of the increase in the common disorders of the alimentary tract—appendicitis, cholecystitis, peptic ulcer—might possibly be attributed to this large-scale tampering with the natural foodstuffs. The authorities in this country and the United States have taken official cognizance of the problems associated with the chemical treatment and contamination of food. Congressional inquiries into the nature of chemicals to be permitted in bread and the problem of chemical residues in food have been published as very bulky verbatim reports. Inquiries on a more modest scale are being conducted in this country, and the Scientific Advisory Council has discussed the question in its latest report.[2] One group of problems results from the increasing use of chemicals in modern agricultural and hygienic practices. Traces of these chemicals may be found in food, and, in fact, a recent report[3] has shown that as much as 30 parts per million of D.D.T. has been found in the fat of Americans whose work did not bring them into contact with the insecticide. No special deleterious effects have been noted in animals that have had D.D.T. stored in their fat for long periods, and in a paper published in last week's *Journal* (p. 819) Cameron and Cheng reported that rats given up to 36 mg. of D.D.T. per kg. of body weight daily for over a year showed no lesions that were characteristic of chronic poisoning with D.D.T. Nevertheless, in view of the biological activity of D.D.T. and the continuous turnover of fat depots, it is difficult to dismiss completely the possibility that the D.D.T. might disturb the metabolic processes of the body.

The substitution of non-nutritious chemicals for natural sugar or fat savours much of the practices of 100 years ago, and there would seem to be no reason for reversing the verdict of the older authorities who utterly condemned these practices. Allowances might be made in times of national emergency when the proper ingredients are scarce, but the distribution of any substitutes for such important foods should be under the control of the Government, so that there is full information about the extent to which substitution is taking place. Foods containing these materials should be so labelled. Similar considerations apply to the use of synthetic dyes, whose unnatural hues should deceive no one into believing that raspberries, lemons, or chocolate, for example, are in any way responsible for the colour of the food purchased. Much greater anxiety is now shown in the "processing" of food, and here the handling of wheat and flour occupies the centre of the stage. It is difficult to believe that the insipid starch sponge sold as white bread really earns the alternative title of "the staff of life." Yet we are assured that this is what the public wants, even though a minority craves for something more palatable—a minority which will heartily endorse Sir Edward's plea that wholemeal bread and flour be made more freely available. Some of the millers' steel rollers might well play

1 *Hansard*, July 4, 1951.
2 *Fourth Annual Report of the Advisory Council on Scientific Policy*, 1950–1, H.M.S.O., London.
3 Lang, E. P., Kunze, F. M., and Prickett, C. S., *Arch. Ind. Hyg.*, 1951, 3, 245.
4 *British Medical Journal*, 1946, 2, 885, and 1947, 2, 298.
5 Flithorn, A., Johnson, D. M., and Crosskey, M. A., *Lancet*, 1949, 1, 143.
6 *Brit. J. Nutrit.*, 1951 (in press).
7 Black, N. McG., and Bennett, J., *Proceedings of the Ninth World's Poultry Congress*, 1951.

a more direct part in the rearmament programme. Nutritionally there is nothing to commend in the activities of those who separate the starch from all the other valuable nutrients of the wheat grain. It is sometimes argued that milling provides a valuable food for pigs, but the separation of the two elements of the grain creates nothing, and both man and his pigs might be better for getting their proper share of the whole grain. Though the millers may be anxious to feed the pigs, chemical manufacturers in the U.S.A. are trying to persuade the baker to substitute synthetic chemicals for lard—and indirectly to reduce the need for fat pigs. Sir Edward Mellanby rightly draws attention to the continued use of nitrogen trichloride for the treatment of flour, despite the confirmation of his pioneer research, which demonstrated convincingly that part of the wheat protein is converted into a substance that is poisonous to all species of animals.[4] There are great differences in the susceptibility of the various species, and no one knows how man compares with animals: one experiment indicated that children were not unduly susceptible to agenized flour.[5]

Few would recommend applying compulsion in order to ensure that the public is offered only what acknowledged experts on nutrition consider to be a more wholesome article than that which the customer appears to want. With domestic animals there are no such scruples, for King[6] has pointed out how closely the composition of their food is controlled by laws and regulations. While the provision of food in its natural state is obviously desirable, it may be impossible to supply this to huge industrial aggregates of population far removed from the sources of their food. It is the need to preserve and conserve food stocks that accounts for some of the contamination and manipulation that takes place. The dangers to health that may result from the chemical manipulation of food cannot yet be exactly defined, and therefore lack of knowledge restricts the power to control it. Sir Edward complains that nothing has yet been done in this country to stop the use of "agene." In America chlorine dioxide has been substituted for nitrogen trichloride, and its use has been recommended in this country. But the substitution of one chemical for another is not necessarily the best answer, and a search is in progress in this country for other agents, physical or chemical, that may have a similar effect as improvers without the risk of producing drastic chemical changes in the composition of the wheat protein. The danger from residues of insecticides or other chemicals used to check damage or destruction of food by pests should recede with a better understanding of the place of chemicals in insect control. Those most in a position to speak with authority on entomological problems have repeatedly emphasized that in agricultural as in medical practice efficient hygiene is the rational and best method for the control of insect pests. Another possible source of danger is the chemical "manipulation" of live animals—for instance, the chemical caponization of cockerels with synthetic oestrogens. Such evidence as exists indicates that the consumer need fear no harm from this practice.[7]

There have been repeated calls for the establishment of some national institute where toxicological problems associated with the increasing use of chemicals in industry and other fields, including food production, can be studied. Sir Edward suggests that a counterpart of the Food and Drug Administration in the U.S.A. should be established. Tremendous efforts have been made there to solve these problems, but the real scientific knowledge that has resulted from all this work is meagre. Some think it is a waste of effort that anyone with a scientific training should spend time trying to decide whether a completely foreign chemical substance such as an artificial sweetening agent is safe to use. Much of the work consists of long feeding tests on the experimental animals, but the results can be strictly applied only to these animals—usually rats—and rarely is time devoted to the study of the mode of action of any of these substances. The design of the experiments is difficult, for it is unrealistic to try to draw conclusions from the results of experiments where rats have been given a substance as, say, 5% of their total diet when it is intended to include only 0.1% in a single article of food for human consumption. Had similar experiments and reasoning been applied to the study of vitamins some would be considered too toxic for inclusion in human food. In such a wide field of experimental testing there need be no shame in accepting the results of routine tests done on a characteristically generous scale by our American colleagues. The Scientific Advisory Council recommends that the Medical Research Council should be responsible for keeping the problem under review and that funds should be provided to set up an information service with close links with similar agencies overseas. Thus there may be no fear that there will be any failure in this country to initiate research on fundamental problems when the need has become evident. The Scientific Advisory Council suggests that an institute devoted to this kind of toxicological testing should be financed by industry—a proposal which might have a number of advantages and safeguard workers at the institute

against being flooded with requests for testing compounds unless there was good reason to believe that they would prove of some value.

Sir Edward Mellanby has expressed his misgivings about the possible effects upon the nation's health of the consumption of many artificial foodstuffs. Evidence of specific deleterious effects will usually be difficult to obtain, but his words serve to remind us of the need for vigilance and for continuous information about the scale on which these manipulations are taking place.

G.P.s' REMUNERATION

Much progress has been made in the negotiations on general practitioners' pay, which began with the Special Conference on July 19. The Conference resolved[1] that the Minister of Health should without delay refer to arbitration the determination of the proper size of the central pool, "having regard to the recommendations of the Spens Report and to present-day money values." The Minister having agreed to arbitration, the questions how it should be undertaken and what the precise terms of reference should be have since been discussed between the General Medical Services Committee, as the executive body of the Conference, and the Minister of Health or his officials. After a certain amount of inevitable sparring, the two parties have agreed on the terms of reference. The Minister suggested that a single adjudicator rather than a court should carry out the arbitration; the G.M.S. Committee accepted this proposal provided that agreement is attained on the name of the adjudicator.

The agreed terms of reference are set out in the Supplementary Report[2] of the G.M.S. Committee to the Annual Conference. It will be seen that they endorse the need to stick to the Spens recommendations. From that basis the size of the central pool is to be determined in accordance with the change in the value of money since 1939 and with increases that have taken place in the incomes of other professions. In addition, "all other relevant factors" are to be included.

Meanwhile, in response to the Conference's resolution on how the newly determined pool is to be distributed, parallel discussions have been held between the Committee and the Ministry, and they have agreed to set up a joint Working Party to look into this. The terms of reference for the Working Party have also been agreed, and here again Spens is the starting point: "To secure an equitable distribution of the central pool based upon the recommendations of the Spens Committee, the object being to enable the best possible medical service to be available to the public, and to safeguard the standard of medical service by discouraging unduly large lists; at the same time, to bring about a relative improvement in the position of those practitioners least favourably placed under the present plan of distribution, to make it easier for new doctors to enter practice, and to stimulate group practice." The Committee rightly made a point of insisting that the basis of the terms of reference must be the Spens recommendations.

There is nothing revolutionary about these aims and they already command widespread assent among general practitioners. In effect, they are an attempt to repair the damage done to general practice since the Health Service began, for the problems they are to solve hardly existed in the old days under National Health Insurance and private practice. They nevertheless present difficulties under the existing scheme of things, and no short cuts to the right answers are likely to be found. In any case the adjudicator's decision on the proper size of the central pool is to be made public as soon as it is reached, whether or not the Working Party has completed its task, and the Minister has acknowledged that finality cannot be achieved in the Working Party until the size of the pool is known. These are important features of the negotiations, and the G.M.S. Committee was wise to insist on them, for they ensure that the Working Party shall not be impelled by unseemly haste to reach an agreement that is later found to be unsatisfactory, and also that the Ministry shall not delay this aspect of the negotiations in order to delay the decision on the size of the pool.

In addition the Committee has obtained from the Minister an assurance in general terms that, in the unlikely event of the Working Party disagreeing, arbitration on this disagreement would not be excluded.

The G.M.S. Committee has a hard task immediately before it, for much of the evidence has to be collected to lay before the adjudicator, and many meetings loom ahead. Doctors are naturally eager to know all that is being done about these vital issues, but a certain reticence in releasing news is imposed upon the Committee by the fact that discussions with a Government department are bound to be largely confidential until some conclusion is reached. Confident that it has so far correctly interpreted the profession's wishes, the Committee will unhesitatingly appeal to local medical committees for further guidance if the need arises, and will in any case be laying the issues before the Annual Conference of Local Medical Committees on October 31.

[1] *British Medical Journal Supplement*, July 28, p. 29.
[2] See *Supplement*, p. 153.

AMENDING THE N.H.S. ACTS

The decision to make the Amending Acts Committee a standing committee of the Association was, in itself, a general expression of dissatisfaction with conditions of work under the National Health Service Acts. To give voice to dissatisfaction is one thing: to canalize it into positive and constructive suggestions is another. Nothing is easier—and, may we say, more delightful?—than to pour out destructive criticism against something one dislikes, and during the three years that have passed since July, 1948, the columns of the *Journal* have been freely sprinkled with individual grievances about various aspects of medical work under N.H.S. But if these grievances are not fairly met by some co-ordinated effort then the spirit of frustration will grow, and both the medical profession and the public will suffer as a result. The Amending Acts Committee considers that "many of the practical results of the Act are harmful to the best interests of the public and of medicine," and its object is to make the Service not only more economical but one in which all sections of the profession can co-operate with good will. It is essential that whatever Government comes into power at the end of this month this fact should be recognized. The medical profession wishes to make the National Health Service a going concern in which it can take pride and in which it can work in accordance with the highest professional traditions. And in this wish it comes into no conflict with the public, because the people of this country cannot possibly get all that is best in modern medicine until those who are providing it are working in harmonious co-partnership with the State. But it is idle to pretend that harmony prevails to-day, or that there is not a widespread feeling of frustration and dissatisfaction, especially among general practitioners. Over the next few years far-reaching changes will have to be introduced into the National Health Service if it really is to fulfil its objects, and the medical profession will have to be unceasing in its efforts to mould the N.H.S. into a form that will enable it to give of its best to the community. As a first step in this direction the hard work of the Amending Acts Committee will, it is hoped, be recognized not only by the profession but by the Government.

In this week's *Supplement* the first report of the Amending Acts Committee, adopted in an amended form as a report of Council, sets forth in a series of recommendations some of the changes it would like to see introduced. Its view is that it should seek now to bring about a number of constructive modifications that would be generally approved, and draw attention to other items to be considered later. The Committee goes back again to what was one of the main sources of disquiet before the Appointed Day in July, 1948—namely, the powers of the Minister. For example, Order 1373 issued under the authority of Section 66 of the Act makes it possible for the Minister to determine by regulation the remuneration of those working in hospitals. This raises again the question of arbitration. As those working in hospitals are, while doing so, employees of the Crown, this makes the Crown a judge in its own case, which is something, as learned counsel puts it, "against natural law." Only a few months ago the medical profession could, under the Conditions of Employment and National Arbitration Order 1305, request the Minister of Labour to refer a dispute to the National Arbitration Tribunal, but since the repeal of this and the substitution of the Industrial Disputes Order 1376 this course is no longer open to the profession. It was advocated in the first year of the Service that conciliation machinery available through a Medical Whitley Council should be backed up by an arbitration agreement, to be determined by the General Council. But there is still no agreement on this, more than three years after the Appointed Day.

It may be recalled that in the Committee Stage of the National Health Service Amending Act,[1] two years ago, speakers for the Conservative Party agreed with Mr. Bevan in his view that neither side could compel the other to go to arbitration. But the experience of the profession, exasperated as it is by the continued delays in settling the outstanding dispute over the remuneration of general practitioners, leads it to press once more for compulsory arbitration. Its first recommendation demands that an Amending Act should provide for a National Health Service Court of Arbitration to which Ministers, or the Management or Staff Side of Whitley Council, could refer disputes on terms of service, including remuneration, whether the terms be old or new. In pressing for compulsory arbitration the Amending Acts Committee is supported by high legal opinion. Learned counsel points out that the Crown is not a third party mediating impartially between the medical profession on one side and boards and councils on the other. The proper way, in his view, of settling remuneration and terms of service of doctors in the N.H.S. is by collective bargaining, backed by arbitration in the event of disagreement. It has, of course, been argued that, in the knowledge that arbitration can be enforced, both sides might approach each other through the conciliation machinery of Whitley with a determination to yield little or no ground. It might be argued, too, that demand for arbitration would arise only in the

[1] *British Medical Journal*, 1949, **2**, 145.

event of serious disagreement, and that in such an event neither side would wish to withhold consent to arbitration by agreement. Those who argue thus would be supported by the recent decision of the Minister of Health to meet the wishes of the profession for arbitration on the remuneration of general practitioners. But the reasonableness of Ministers of Health is an incalculable factor, and it is necessary that by some means or another the profession should safeguard itself against arbitrary and one-sided decisions by any Minister of Health on terms and conditions of service. If collective bargaining fails, then arbitration is essential, it being recognized, of course, that in any decision affecting the public purse no arbitrator can usurp the authority of Parliament.

Arbitration is uppermost in the minds of the profession to-day, if only for the fact that it draws attention once more to the great powers conferred by the Act on the Minister of Health. As the Amending Acts Committee points out, of the 79 clauses and 10 schedules in the Act for England and Wales, no fewer than 40 confer on the Minister power to make regulations and orders. In a series of recommendations it seeks to modify these powers. Again in the hospital service the Committee sees in the administrative structure something which is imposed from above downwards rather than something in which power at the top arises naturally from a democratic method of election in units at the base. The recommendations relating to hospital and specialist services suggest that hospital management committees should be democratically elected and not, as at present, appointed by the regional hospital boards, that these committees should have greater executive powers and financial authority, and, too, that regional hospital boards should be elected by, among others, hospital management committees and the medical staffs of the hospitals in the regions concerned. What concerns the Amending Acts Committee is that in the hospital service to-day decisions are taken by remote bodies which can have little knowledge of local needs and difficulties, and it seeks in its recommendations to restore the sense of local interest and responsibility which among other things would promote efficiency and economy. Though it is not easy to see from the Committee's report what would constitute the electorate and how practicable these recommendations would be, the motive behind the recommendations will receive widespread approval. It is essential for the efficiency of the hospital service that responsibility should be progressively devolved upon those who actually have to provide services for the community in which the hospitals exist. The Committee criticizes the curious system of hospital finance whereby each regional hospital board has to submit in advance a detailed estimate of every item of expenditure to be expected in the coming year. At present it is not possible, in the light of experience, to transfer expenditure granted on one item to another, nor is it possible to carry forward to a subsequent year money not expended in the year estimated for. This is a system which leads to extravagance and inflexibility. The Amending Acts Committee advocates a scheme of block grants for hospital finance, the grants to be made to hospital management committees. It advocates, too, that surpluses should be carried on from year to year. Another point stressed on the hospital side of the Service is the need for constant joint consultation at all levels, and in this consultative machinery general practitioners and medical officers of health should be represented. Other recommendations refer to private beds in hospitals and to drugs and appliances for private patients. It certainly seems anomalous that private patients who support the Service out of income tax should be deprived of any part of it, and if, for example, the Government were to do what has been advocated by many—namely, to make free to all indispensable drugs while requiring the public to buy household remedies direct from the chemist—then such a recommendation put into effect should not increase the cost of the pharmaceutical service.

The report of the Amending Acts Committee will be considered by a special meeting of the Representative Body on December 13, and it is possible that as a result of the debate on that day some of these recommendations may be changed. What is important is that a first step has been taken to attempt to modify the National Health Service, and it is hoped that after the Representatives' meeting those recommendations which are practicable and secure general consent will be supported vigorously by the whole profession. Three years of experience of the N.H.S. has shown doctors in this country that in spite of their efforts to make it a success the machinery still groans and creaks. It badly needs overhauling, and until it has been overhauled we shall not be able to say either to the people in this country or to the rest of the world that the National Health Service is a success. In fact, unless its finances are reorganized it will turn out to be a costly failure, and it is to everyone's interests to see that this is not so.

FLIES VERSUS CHEMICALS

In the past six years D.D.T. and other synthetic insecticides have been used on an exceptionally large scale. It is encouraging, therefore, that so few reports have been made of insects appearing resistant to these chemicals

after extensive and regular control operations. The best authenticated cases of resistant strains seem to be in one or two species of Culicine mosquitoes and in the housefly. Resistant houseflies have been reported from many parts of Europe and North America, but, curiously enough, the housefly of the Tropics (*Musca nebulo*) does not seem equally capable of developing resistance[1,2] though D.D.T. spraying there has been more widespread. Resistant flies of the type *Musca vicina* have, however, appeared in such sub-tropical areas as Egypt[3]; so that the phenomenon is not restricted to *M. domestica* in the temperate zones. Resistance to insecticides is not necessarily absolute, but the flies can withstand many times the dose lethal for normal flies. (The exact ratio depends on the method of assessment: conservative estimates are 10 to 100 times the dose, but figures like 10,000 have been published.) For practical purposes it is sufficient that wall spray treatments are quite inadequate for controlling resistant flies.

It seems likely that the phenomenon of resistance originates in fly populations with a few members possessing innate and inheritable tolerance, far in excess of the normal minor differences in individual tolerance observed in all species. Obviously, the wide use of insecticides soon brings the progeny of such flies into predominance, by selective mortality. The usual sequence of events has been that the early D.D.T. house-spraying campaigns have successfully controlled houseflies, and (e.g. in Italy) have been reported to reduce fly-borne summer diseases; but that after one or two seasons D.D.T. fails to control the flies, though laboratory tests show that they are still susceptible to other synthetic insecticides. Other compounds are then used in the field, successfully at first; but within two years or less the flies become highly resistant to these too.

So far, resistance in the field has developed only towards certain chlorinated hydrocarbon insecticides, but it is nevertheless clear that there are several types of resistance. Apart from differences in the particular compounds tolerated, some strains are paralysed by D.D.T. and recover, while others seem to be quite unaffected.[4] The protective mechanism at work is not completely understood. It is certainly not a simple matter, such as avoidance of the poison or possession of an impermeable cuticle, for resistant flies will tolerate high doses of D.D.T. injected into their bodies. The most promising theory is that the tissues of these flies are able to destroy the D.D.T. by a process of dehydrochlorination.[5] Experiments show that they are able to do this much faster than normal flies, but the detoxifying mechanism is at the best very slow, and resistant flies can survive with much more than the normal lethal dose of D.D.T. inside them, so that this cannot be the complete explanation.

The capacity for tolerating insecticides is inherited, but genetical investigations have given conflicting results. An American study[6] suggests a multiple factor inheritance, while a British study gave clear indications of inheritance through a single gene, susceptibility being dominant.[7] Different measures of resistance were used (lethal dose, and paralysis time) and it is possible that these two different characteristics of flies may be inherited in different ways.

Resistant strains of fly remain resistant in captivity, in the absence of D.D.T., for very many generations. Various workers have reported a more or less slow decline in average resistance, apparently for the reason that the proportion of susceptible individuals slowly rises, presumably because they have a slightly better chance of survival in the absence of D.D.T., at least in the laboratory, than do resistant individuals. But it is impossible to judge whether this happens in nature, or how rapidly a large resistant population would become diluted by susceptible flies. It seems unlikely that it would be quick enough for successful control by ringing the changes among various synthetic insecticides; especially as it has been observed that strains already resistant to D.D.T. develop resistance to other synthetic insecticides more rapidly than "normal" fly populations. Furthermore, selection for one insecticide may induce resistance to other compounds. In Sardinia the wide use of D.D.T., followed by "chlordane" for several years, resulted in flies resistant to "dieldrin," "aldrin," and "toxaphene," none of which had been used on the island.[4]

The practical future of fly control seems to lie in a return to sanitation, poison baits, and pyrethrum sprays, methods on which we relied before the introduction of D.D.T.

1 Busvine, J. R., *Ceylon J. med. Sci.*, 1949, (D) **4**, 1.
2 Pal, R. R., *Trans. R. Soc. trop. Med. Hyg.*, 1951, **45**, 125.
3 Graham, J. B., *et al.*, *Science*, 1950, **111**, 651.
4 Busvine, J. R., *Nature, Lond.*, 1951, **168**, 193.
5 Sternberg, J., *et al.*, *J. econ. Ent.*, 1950, **43**, 214.
6 Bruce, W. N., *et al.*, *Soap*, 1950, **26** (3), 122.
7 Harrison, C. M., *Nature, Lond.*, 1951, **167**, 855.

PULMONARY EMBOLISM DUE TO AMNIOTIC FLUID

Pulmonary embolism due to amniotic fluid was first described as one of the possible causes of obstetric shock by Steiner and Lushbaugh[8] 10 years ago. In the typical case the victim is an elderly multigravida, often of short and stocky build, who has been in strong or even violent labour with a large foetus. The onset of symptoms has, except in one case,[9] occurred after the rupture of the membranes—usually during labour, less often after its conclusion, and exceptionally before labour has started.[10] In many cases the liquor amnii has been noted to contain blood or meconium or both. The clinical picture is one of a preliminary chill rapidly followed by profound shock with dyspnoea and cyanosis, the patient dying within a few minutes or hours. The characteristic post-mortem findings are in the pulmonary arterioles and capillaries, where emboli are found consisting of the particulate matter of amniotic fluid and, in some cases, meconium. Thus desquamated epithelial cells, mucus,

8 *J. Amer. med. Ass.*, 1941, **117**, 1245.
9 Steiner, P. E., Lushbaugh, C. C., and Frank, H. A., *Amer. J. Obstet. Gynec.*, 1949, **58**, 802.
10 Crowder, R. E., and Bills, E. S., *ibid.*, 1950, **60**, 1389.
11 Shotton, D. M., and Taylor, C. W., *J. Obstet. Gynaec. Brit. Emp.*, 1949, **56**, 46.
12 Mallory, G. K., Blackburn, N., Spurling, H. H. J., and Nickerson, D. A., *New Engl. J. Med.*, 1950, **243**, 583.
13 Gross, P., and Benz, E. J., *Surg. Gynec. Obstet.*, 1947, **85**, 315.
14 Seltzer, L. M., and Schuman, W., *Amer. J. Obstet. Gynec.*, 1947, **54**, 1038.

and lanugo hair may be seen together with many leucocytes about and within the emboli. Similar emboli have also been found in the capillaries of other organs, including the heart, brain, and kidneys,[11 12] while in patients on whom post-mortem examinations have not been performed the embolic material has been recovered from blood aspirated from the right ventricle of the heart.[13] In about half of the reported cases obvious tears into the myometrium from the interior of the uterus have been found; epithelial cells have been demonstrated in the uterine sinusoids and pelvic veins of the majority. The route of the emboli is thus clear, and indeed Steiner and Lushbaugh caused similar clinical and pathological signs in dogs and rabbits by the intravenous injection of meconium and of unfiltered liquor amnii. The injection of filtered amniotic fluid was without effect, which indicates that the contained particulate matter is the danger.

Fewer than 25 cases of this form of embolism have been reported, nearly all of them fatal. In at least one-quarter of them other abnormalities which made death more likely, notably rupture of the uterus, were found after death. In the absence of other adverse factors, however, the patient may recover, and non-fatal forms of the disease have in fact been recognized clinically.[14] Pulmonary embolism from amniotic fluid should be suspected in the presence of sudden and unexpected shock in labour, and, while no specific form of treatment is known, morphine and atropine may be administered. When the pathogenesis is considered, it is not surprising that this particular complication of labour does occur; rather is it surprising that it apparently occurs so infrequently.

GUIDE TO CENSUSES

That numbers are rigorous abstractions from what they enumerate is one of their main features of interest to medical men. Remotely yet exactly descriptive, by means of them comparisons can be made that are impossible in any other way. Though the difficulty of making valid inferences from such comparisons is well known to anyone who has worked on the mass of data collected at censuses in Britain during the last 150 years, the chief problems that the census figures initially set statisticians are whether people have correctly stated the facts on their census schedules, and whether identical definitions of occupation, infirmity, and so on refer to the same conditions in successive censuses. A third and different kind of problem is knowing where to look for the information that has been gathered, for many of the questions have varied from one census to another.

An exceedingly helpful booklet has now been published[1] giving information of this kind in succinct form. Prepared by an Interdepartmental Committee, presided over by Dr. George North, the Registrar-General for England and Wales, it describes the questions asked at every census from the first in 1801 (with the exception that the 1951 census is only briefly touched on), how the answers were obtained from the population, and how reliable they are. After introductory sections on the methods of census taking and on conclusions that may be drawn from the population figures, the committee discusses in detail the subjects selected for special inquiry at the various censuses. We learn, for example, that in 1801, when the census was carried out by enumerators, these officials were asked to classify the occupations of the people in their areas into three classes—agriculture; trade, manufacture, or handicraft; and others. In 1831 there were seven categories, and doctors would then have come into the class of "capitalists, bankers, professional or other educated men." A century later the classification was into some hundreds of categories, including one for the temporarily unemployed.

In censuses taken from 1851 to 1911 attempts were made to elicit information about certain physical and mental infirmities such as deafness, blindness, deaf-mutism, and mental deficiency. The questions were subsequently discontinued because, though the data obtained were of some slight value, the census was found not to be a suitable medium for getting information of this kind. In 1911 a direct inquiry into the fertility of marriage was made for the first time. It was not repeated in 1921, but in 1931 an inquiry of restricted scope was held. The booklet abounds in reference information of this kind which will clearly save a great deal of fruitless searching—when, for example, an inquirer wants to compare with past experience the fertility data obtained at this year's census.

The errors that hedge the figures about because of the misstatements returned on the census forms command a wider interest than merely the statisticians', and this booklet refers to a number of them. Many people are dissatisfied with the age they have attained—even if they know it, and many do not. It has been found that too many ages end in 0 and too few in 1. This is of practical importance to medical men, for, since the excess in the first group about equals the deficit in the second, the two should be included in the same five-year age group if cases are being so classified: that is, quinquennial age groups of a series of, say, hospital patients being studied should run 20–24, 25–29, 30–34, not 21–25, 26–30, 31–35, as is sometimes seen. Other errors include an excess of women between the ages of 20 and 30, while the elderly are apt to assume a more distant birthday than their mothers would warrant. These are features of human aspiration rarely taken into account when recording medical statistics from hospital or other data. Another factor responsible for errors is failure to understand the question—with which medical students will sympathize. In the census of 1911 a woman aged 21, married for one year, was recorded as the mother of seven children who were presumably born to the husband by a previous wife.

This excellent guide is the second in a series, the first having been on labour statistics. The committee or some other body, such as the Registrar-General's department, might well consider preparing on similar lines an up-to-date guide to the Registrar-General's many other regular publications on vital statistics. It would surely be welcomed.

[1] *Census Reports of Great Britain, 1801-1931.* H.M.S.O., London. 1s. 3d.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

CHRONIC ILL-HEALTH AND RESPIRATORY INFECTION IN CHILDHOOD

BY

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There is a very common picture of general ill-health associated with chronic or relapsing respiratory infection, and having its greatest incidence in the first years of school life. It comprises at least one-fifth of the cases referred to children's out-patient clinics and is well known to all who conduct such clinics; indeed, it must be well known to every doctor. It suffers, however, from being not readily amenable to academic description. It is too diffuse and vague, and includes too many cases differing in detail, to fit the concept of disease entity or even syndrome. If it is divided into parts or narrowed down to "sino-bronchitis" much of the essentially composite picture is lost.

There is a basis of general debility and fatigue, recurrent colds, and recurrent or persistent cough. Added to these are the various other manifestations of minor or borderline ill-health—pallor, poor or fickle appetite with failure to gain weight, indigestion and bilious attacks, and interference with sleep. Added, too, are the multiple minor abnormalities of behaviour which become so much more apparent in the child who is never really well. There is usually a postural defect which tends to be particularly marked in the child of asthenic physical type.

Besides varying in detail, the picture varies greatly in degree, merging on the one hand with the normal and on the other hand with its more clearly defined complications. Probably about one-fifth of the children at this age in England present clinical or radiological evidence of some persisting upper respiratory infection, and only a small proportion of children at this age could be described as having perfect posture. The decision on where definite illness emerges must be an arbitrary one.

With this uncertain outline, it is not surprising that the picture, common, well known, and troublesome as it is, does not receive much attention as such in the modern textbook, though if we look back to the more discursive, less precise books of 50 years ago we find detailed descriptions in plenty. Eustace Smith in 1899 described these children as suffering from "mucous disease." He noted the greenish yellow mucus in the back of the throat, and thought that their multiple symptoms and chronic ill-health were due to failure to absorb adequate nourishment owing to similar mucus lining the whole digestive tract. G. F. Still thought the cause was infected adenoids, and this is still believed by many people. Sir Robert Hutchison quotes Eustace Smith in giving his own vivid description, but does not altogether accept either the "mucous disease" theory or the adenoids. He emphasizes the importance of considering the whole child and his surroundings and especially his diet.

It is suggested that it may still be a reasonable idea to attempt a general account of these children in terms of the development of their illness and of its treatment.

Development of the Picture

A shooting-up stage in growth occurs during the first years of school life. The rounded limbs and body of the toddler change to ribs that "stick out" and "skinny" arms and legs. This normal change has long been commercialized, and itself may cause anxiety and unnecessary treatment. At the same time it is a stage during which the normal erect and alert posture and carriage can easily droop and slump with any illness or with any minor cause of fatigue.

Also at this time usually comes the first massive contact with the cross-currents of respiratory infection, and frequent colds are so common an accompaniment to starting school as to be almost a normal course of events. It is when infection settles in a mild chronic form in one or more of the nasal sinuses that the picture of persistent ill-health may gradually emerge. Cold follows cold with quite abnormal frequency—"He's no sooner rid of one than he starts another." A persistent cough, usually noisy and ineffective, becomes established both at home and in school, and disturbs sleep at night. The tired droop becomes a persisting postural defect—a kyphoscoliosis with widely separated scapulae, forward sloping head, and open mouth. This habitual position further impairs the proper function of the respiratory passages, so making infection more likely to persist.

Cough is probably the commonest presenting symptom. One may presume that mucopus in the nasopharynx is the commonest cause of cough in childhood. Cough and mucopus there are so very commonly associated, and the cough stops when the nasal infection has cleared. Also, iodized oil of about the same viscosity as mucopus placed in the nose at night can be radiologically demonstrated in the lung fields next day.

The full picture of ill-health may develop slowly or rapidly and, once the vicious circle has become established, may persist for months or years, improving a little in the summer or after a holiday by the sea, becoming as bad as ever after a fresh recrudescence of infection or an attack of measles or pertussis, and continuing in a mild chronic form or with more acute episodes of febrile bronchitis. Sometimes other symptoms, abnormalities of behaviour, or periodic episodes with fever and pallor, or headache and vomiting, may take chief place in the parents' story against a background of cough and colds and general failure to thrive. A minority develop the more serious or clearly defined complications. Segmental collapse-consolidation may present acutely as pneumonia, or bronchiectasis may slowly appear, though the latter is more common when respiratory infection dates from infancy. Recurrent attacks of follicular tonsillitis may occur independently, but are often associated with sinus infection, as is middle-ear inflammation. More commonly the tonsils and adenoids undergo the degree of hypertrophy which seems to be

normal at this age, without themselves being the seat of any obvious infection or necessarily having any bearing on the problem.

Examination and investigation are simple procedures. The pallid round-shouldered child does not require further general description. Mucopus may be visible in the nose, crusted in the handkerchief, or as a greenish-yellow drip on the posterior wall of the pharynx. There may be some rales at the lung bases which will often disappear after coughing or a few deep breaths. In the great majority of cases no radiological or other hospital investigation is required in the first instance. A haemoglobin estimation and a tuberculin test are useful in any indefinite state of ill-health in childhood, and, together with the simple testing of urine, can and should be carried out by the general practitioner or the school medical officer. It is unusual for a radiograph of the sinuses to give evidence of infection which is not apparent on careful examination of the upper respiratory tract by ordinary methods and with ordinary equipment, and a radiologically opaque antrum may sometimes be shown not to be infected. A radiograph of the chest is not needed unless there are persistent chest signs, or symptoms in spite of treatment, when an area of collapse is to be suspected. Many of these children nevertheless do become chronic hospital out-patients, their case-note envelopes becoming thicker with the years and their *x*-ray covers stretching to bursting point.

Ultimately, recovery to normal health in the filling-out stage of growth which precedes puberty is the general rule; but in many cases there is a residual catarrh which persists as a slight impairment of health in adolescence, or there may be a degree of permanent postural defect.

Treatment

There is probably no group of cases in which treatment as generally carried out is so irrational and ineffectual. These children constitute the main market of the industries producing the vast quantities of cough mixtures which are still used, the tonic vitamin preparations, and the jars of malt syrup which most of us remember from our own childhood. Cough mixtures and vitamin tonics are still the first line of treatment usually adopted by the doctor, though there is no evidence that cough mixtures have any therapeutic value in these cases or that vitamin deficiency now plays any part in causing this sort of ill-health. Medicines containing alkaloids of the morphine and atropine groups, by diminishing secretion and making it more viscid, may make bronchial plugging more likely and so may do harm. It is difficult to see what possible good the malt syrups can do, though they do at least taste pleasant and are a firmly established part of tradition.

Rational treatment of this very common picture presents a problem in co-operation and should have three main aims: rest, nasal treatment, and exercises.

Rest

There is an obvious element of fatigue, and adequate rest in the often overcrowded, wireless-ridden homes of to-day may be difficult to obtain. Adequate rest means early to bed, and for younger children a short rest after the midday meal and the occasional old-fashioned day in bed.

Nasal Treatment

Sinus infection usually clears up on treatment with 1% ephedrine and 1% mild silver proteinate *B.P.* in saline used as nose drops twice or thrice daily for a period of about six weeks. That this has a decongestive action favouring drainage, and also slightly increases secretion, can be observed, and it has been shown to do no harm. Treatment must be carried out regularly with the head held vertically downwards and backwards (see illustration), about

Photograph showing how to instil nasal drops.

half a dropper-barrelful of the solution being used each time. Substances instilled into the nose too often find their way over the upper lip or face, or along the floor of the nose and straight into the pharynx, so the proper technique is important. There is little discomfort, and almost all children accept the treatment without difficulty. The course may need to be repeated some months later. If, in spite of this, infection persists, treatment by irrigation or displacement under the care of an ear, nose, and throat surgeon may be required, and this may be combined with medical treatment such as a course of a sulphonamide preparation, depending on the organisms found in the washings.

Removal of tonsils may be indicated by the occurrence of several observed attacks of tonsillitis, or removal of both tonsils and adenoids when, as uncommonly happens, they are so hypertrophied as to cause obstructive symptoms and signs.

In most cases of nasal infection, if treatment with ephedrine and the mild silver proteinate is carried out with real thoroughness and attention to detail it restores adequate drainage and the sinus infection clears up without any further trouble.

Exercises

These aim at restoring normal posture and normal breathing, and consist mainly in rhythmical breathing and swinging and stretching movements which are best done in small classes. Their success is acutely dependent on the ability and personality of the instructor, and they can easily become a useless ritual. In addition there should be improvised feats and games, using wall bars, the climbing frame, and the climbing net. Normal posture is ultimately dependent on righting reflexes, and it is through these that climbing and feats involving balance help to restore the normal.

Exercise on these lines should be given at first once or twice weekly, and later for a short period of about half an hour daily. The simple equipment and instruction required should ideally be a part of every school, when all that would be required would be some special attention to the individual child. As it is, the provision of exercises without too much loss of school time is the greatest difficulty, though the problem and the possibilities are being considered, as can be seen in the Ministry of Education's report *The Health of the School Child* published in 1949.

Rest, nasal treatment, and exercises are needed in every case. In a few cases anaemia will need treatment,

or orthodontic treatment may be required, and in a few also, where home circumstances are very bad, a period of convalescence may help.

It is all-important to ensure that the three main aims in treatment are followed simultaneously. The posture will soon relapse if a chronic nasal infection is allowed to continue, and nasal infection will soon recur in the child whose drooping shoulders and open mouth have remained uncorrected, while both treatments will fail in the child who is chronically overtired as a result of his illness.

When such combined treatment is possible a return to full normal health can usually be expected in three to four months.

CHEMICALS IN FOOD

The Food, Agriculture, and Fine Chemicals Groups of the Society of Chemical Industry held a Joint Conference at the Wellcome Research Institution, London, N.W.1, on September 27 and 28 under the general title "Problems Arising from the Use of Chemicals in Food." Twelve papers, dealing with a wide variety of deliberate and incidental additives, were presented and discussed. Special consideration was given to the possible effects of additives on man and to their desirability in food processing and handling.

In his opening address, Dr. G. ROCHE LYNCH reviewed the history of the use of chemicals in food. Accum's treatise on the subject of adulteration (1820) had been the forerunner of others which had culminated in the Food and Drugs Act, 1860. There then had followed a period of well-meaning though unenlightened use of such preservatives as boric acid and formaldehyde, but abuses had developed. To-day the prime reason for the use of additives was the world shortage of food. They were used to increase production and to facilitate processing and the efficiency of the necessary marketing operations of packaging, storage, and transport. In the consumer's interest controlling legislation was needed for the large number of different types of chemicals now in use; nevertheless, reputable food manufacturers were taking an active interest in the problem and were keen that "good commercial practice" should be observed.

Dr. H. E. COX said that the physiological action of many of these surface-active agents, which had to some extent displaced gums, lecithin, and egg yolk, was largely unknown. They had little or no food value, but could be used to replace as much as 50% of the fat required in some products: this, however, was regarded as a misuse in normal times, when they should be used solely to obtain satisfactory mixtures and dispersions. Amounts added rarely exceeded 1%, and were usually much less. Ethylene glycol was not recommended, and further work was necessary on acetyl-tartaric acid, polyoxyethylene, and sorbitan esters. It was doubtful, also, whether ethanolamines, morpholine, pentaerythritol, or their monoglycerides, were suitable for inclusion in foods.

Preservatives

Dr. F. H. BANFIELD said that it was unreasonable to condemn synthetic additives simply because they were synthetic. Work on any new additive should include a study of its acute and chronic toxicity, its absorption and metabolism, the mode and rapidity of its excretion, and its effect on other food constituents and their metabolism and on the alimentary micro-flora. Preservatives should never be used for unreliable products or to cover careless handling. Of the commoner preservatives benzoic acid was not cumulative in effect, and amounts up to 0.5 g. a day seemed harmless; sulphur dioxide was excreted rapidly, and an adequate safety margin was provided in its permitted uses. Propionates (as anti-mould agents), *p*-hydroxybenzoic esters, and ethyl vanillate had proved satisfactory in toxicity trials. Dehydroacetic acid was of doubtful toxicity. The use of antibiotics in food processing must be viewed with great suspicion.

Antioxidants

Dr. C. H. LEA distinguished true antioxidants—for example, polyphenols which act as chain breakers in the autoxidative processes—from synergists which enhance the activity of the former. A further class included agents which form inactive complexes with copper, manganese, or iron. Many polyphenols occurred naturally in foods, and others were introduced during the process of smoking meat and fish. The artificial addition of antioxidants was now practised in the United States. Tocopherols, citric, ascorbic, and probably gallic acids, and lecithin occurred naturally, so that their addition presented no new circumstance. The addition, as antioxidants to food, of about five phenolic and five non-phenolic substances had recently been permitted in the U.S. after comprehensive acute and chronic toxicity tests. But on similar grounds hydroquinone, catechol, and thiourea had not been permitted. Of the purely artificial compounds the thiopropionic esters and the tetra-alkylthiuramdisulphides had been shown to have low toxicities.

Manipulation of Flour

Dr. A. J. AMOS explained that the reason for adding improving and bleaching agents to flour was to effect promptly beneficial and desirable changes in flour properties which could be achieved only slowly by natural means—that is, to effect an artificial "ageing." The use of yeast foods by the baker allowed the bread-making potentialities of a flour to be developed to the full and a more uniform standard of bread quality to be maintained. These treatments enhanced the nutritional importance of bread, which to-day provided over 30% of our protein and contributed significantly to our vitamin requirements. Following the discovery that nitrogen trichloride could give rise to canine hysteria, the remaining commercially used improvers and bleachers and the officially favoured replacement for nitrogen trichloride—namely, chlorine dioxide—had been subjected to extensive and stringent feeding trials not only with animals but also with human subjects, and not one of them had given the slightest evidence of constituting a hazard to health.

Colours and Flavours

Dr. P. R. PEACOCK's paper on colouring materials was read in his absence by Mr. A. L. Bacharach. Dr. Peacock stressed the importance of the aesthetic appeal of foods, and then developed an argument for the ideal of no additives except possibly those of natural occurrence. In the absence of that ideal state, he drew attention to some of the problems involved. No completely new synthetic chemical could, from its chemical structure alone, be pronounced "safe" with certainty; chemical similarity with other substances was not an infallible guide, though analogy might be used with success up to a point. Carcinogenicity towards animals should bar a substance from human consumption even though the latent period might be much greater in the latter circumstance as with β-naphthylamine. Bioassays were lengthy, but Miller's recent work on the fixation of carcinogens by liver protein might be developed to advantage. In the ensuing discussion emphasis was laid on the excessive doses of carcinogens and potential carcinogens fed to animals over prolonged periods: in similar experiments, sodium chloride would probably prove fatal.

Concerning flavours, Mr. G. N. REVIE indicated that, because of the high ratio of solvent to flavouring constituents, attention was primarily directed to work on the toxicity of solvents.

Agricultural and Inorganic Residues

Dr. R. A. E. GALLEY said that consumer hazards associated with the use of toxic chemicals in agriculture were

now under consideration by a Working Party of the Ministry of Agriculture and Fisheries. To some extent chemical treatment was necessary for good yields of clean, wholesome fruit and for the storage of infected grain. The chlorinated hydrocarbons, organo-phosphorus and -mercury compounds, and the new sulphur compounds had for the most part an LD50 of less than 1 g./kg. and must accordingly be used with care. So far as the consumer was concerned, however, the risk of poisoning was considerably reduced by a variety of factors—for example, 3:5-dinitro-*ortho*-cresol (D.N.O.C.), 2:4-dichlorophenoxyacetic acid (2,4-D), and methoxychlorophenoxyacetic acid (M.C.P.A.) were applied long before harvesting, by which time they had decomposed or been washed away; tetraethyl pyrophosphate (T.E.P.P.) was rapidly hydrolysed to harmless compounds. 2,2-*bis*(*p*-chlorphenyl)1,1,1-trichlorethane (D.D.T.) accumulated in body fat, but under normal conditions was innocuous; benzene hexachloride (B.H.C.) was less suspect, but the Medical Research Council had advocated a γ-isomer limit of 2.5 parts per million (p.p.m.) for foodstuffs. Parathion inhibited cholinesterase, but an adequate safety margin was provided if it was used not less than a month before harvesting.

Dr. J. T. Martin stated that no consumer hazards arose from the use of rotenone, nicotine, calomel, metaldehyde, or Paris green in consequence of their respective modes of application. Lead arsenate should be used at least six weeks before harvesting, D.D.T. was not officially recommended during or after blossoming, and similar precautions were necessary when using mercury fungicides. "Schradan," a systemic insecticide, decomposed fairly rapidly, 3 p.p.m. being considered harmless; whilst *bis-iso*propylaminofluorophosphine oxide was claimed to be less toxic. Generally, little risk of significant residues seemed likely if the normal recommendations and precautions for application were observed.

Mr. A. T. Parsons drew attention to some less obvious but possible sources of contaminants—arsenic in malt or chicory from flue gases in the drying process; lead, antimony, and fluoride from soft enamels in contact with acid foods; cadmium from plated parts in refrigerators, etc.; and antimony from some compound rubber gaskets. Generally speaking, arsenic, antimony, lead, selenium, cadmium, mercury, vanadium, and molybdenum were inessential to life and harmful; nickel was inessential and harmful in excess; aluminium, tin, and silver were inessential, but probably harmless; copper, iron, zinc, fluorine, manganese, cobalt, and iodine were essential, but harmful in excess.

Processing and Hygiene Aids

Dr. J. B. M. Coppock stressed the importance of developing accurate analytical methods for determining potential contamination from processing and hygiene aids, some of the difficulties being outlined. High viscosity mineral oils were less likely to be absorbed than those of low viscosity. D.D.T. as an insecticide should be used with adequate precautions and contact with foods avoided; B.H.C. was associated with less risk, but might have an adverse effect on dough properties in bread-making. Pyrethrins in conjunction with synergists (e.g., piperonyl butoxide) were considered safe insecticides and were used extensively in the U.S. for multi-wallpaper sacks. The use of quaternary ammonium compounds as detergents and bactericides required careful review. In the latter case they probably acted by cell membrane disruption. They might be absorbed by fats and lead to a position similar to the accumulation of D.D.T. in body fat. It was suggested that the toxicology of these substances at or near the concentrations which had been suggested for their use needed careful review. Polystyrene, polyvinyl, and polyethylene resins, vinylidene chloride, vinyl chloride, and cellulose acetate were considered suitable for wrapping materials, but care was necessary when using di-2-ethylhexyl phthalate with fatty foods.

Pharmacological Aspects

Professor A. C. Frazer distinguished between accidental adulterants and deliberate additives, dealing mainly with the latter. The "health of the public" could only be assessed statistically, being a function of many variable individual and communal factors. Until recently, most food was prepared in the home: latterly an increasing amount of prepared, processed, and pre-cooked food was being consumed. In these circumstances, chemical additives had been used to ensure uniform results and to facilitate distribution. This particular communal factor represented an environmental change dictated by the circumstances of our time. Its effect on public health was unlikely to approach that of, say, the introduction of tobacco or the motor-car. To advocate "natural" as opposed to synthetic chemicals was fallacious. Public health as measured by morbidity and mortality rates had actually improved in recent years. There was in fact evidence that natural foods themselves might be harmful: thus cholesterol-containing foods might influence arterial degeneration, rancid fats might play a part in the aetiology of tropical sprue, and both agenized and non-agenized flour could aggravate the coeliac syndrome.

All additives should be subjected to chemical and physical tests, acute toxicity trials, biochemical studies of their absorption and metabolism and of their effect on the gastro-intestinal tract, chronic toxicity tests in animals, and, finally, human trials. These having been done, a small element of risk might still remain for a "satisfactory" compound; but the magnitude of this would be no greater than that provided by many of the other communal, not to say individual, factors already operative.

There was no evidence that nitrogen trichloride had had any deleterious effect on public health, but it was wise to cease to use it on the grounds of the results of the animal experiments. Polyoxyethylene stearate was essentially non-toxic, but in excessive amounts it might cause diarrhoea: its effect on the gastro-intestinal system should thus be more fully investigated. Glyceryl monostearate and stearyl tartrate appeared to be non-toxic so far as present evidence went.

There was no cause for alarm about the use of chemicals in food. If adequate support were given to basic research in this field, and the materials used were subjected to the investigations proposed, the health of the public could be adequately safeguarded.

Legal and Administrative Background

Mr. C. A. Adams's paper briefly presented the legal position of chemicals in food under the Food and Drugs Act, 1938, with special reference to the advances in the chemistry and technology of food and the additives. The Delaney Report* and recent parliamentary motions were discussed, the advantages and disadvantages of total prohibition reviewed, and attention drawn to certain difficulties of enforcement which were independent of the method of enforcement used: the latter included cost, the assessment of expert evidence, and the dearth of exact knowledge.

Need for a Central Laboratory

In his closing address, Professor H. D. Kay said that a corollary to the arguments heard in the symposium contributions seemed to be the need for the early establishment of a central laboratory with a small advisory board on which should be represented the Ministries of Food, Agriculture, and Health, the Medical Research Council, the Agricultural Research Council, the Society of Chemical Industry, and the Society of Public Analysts. Such a laboratory would have the duties of examining experimentally the properties of all new substances which it was proposed to add to human (or animal) food, and would deal also with the toxicity and other physiological properties of insecticides, etc., used in

*A Select Committee Report to the American House of Representatives. Report No. 3254. January 3, 1951.

agriculture, of synthetic detergents, and of other chemicals which might get into human food. One of the responsibilities of this laboratory might be the preparation of a type of pharmacopoeia in which all non-nutritive chemical substances that were permitted to be added to food should be listed, with methods of analysis and references to the published literature.

It would be on the basis of the considered findings of this laboratory, which might be financed through one of the research councils or the Ministry of Food, that additions to an official list of chemicals whose presence in food was (within defined limits) permitted might be made. The laboratory, apart from its routine work, would also engage in research on new methods of testing and in related physiological and pharmacological science.

THE KING'S HEALTH

STEADY IMPROVEMENT REPORTED

Below we print the bulletins on the King's health issued since Tuesday, October 2, at 11.30 a.m. All these bulletins have appeared over the signatures of the same five doctors—namely, Sir Daniel Davies, Sir Horace Evans, Dr. Geoffrey Marshall, Mr. C. Price Thomas, and Sir John Weir.

Wednesday, October 3, at 11.30 a.m.:

After another good night the King's condition shows further improvement.

Thursday, October 4, at 10.30 a.m.:

The King continues to make steady progress.

Friday, October 5, at 10.30 a.m.:

The King's improvement continues.

Saturday, October 6, at 11 a.m.:

The King gains strength daily. The post-operative period has passed without complication. In view of the seriousness of the operation, progress towards the convalescent stage must necessarily be slow and gradual.

Sunday, October 7, at 10.30 a.m.:

The King has had another good night. His Majesty continues to make satisfactory progress.

A statement issued on Monday, October 8, read:

Since his Majesty's progress has been maintained steadily and satisfactorily it is not expected that there will be another medical bulletin.

WESTMINSTER MEDICAL SCHOOL

The inaugural address for the new session at Westminster Medical School was given by the Vice-Chancellor of the University of Oxford (Very Rev. John Lowe, D.D.) on October 1. Dr. Lowe discussed the perennial problem of body and mind.

In so far as medicine belonged to the biological sciences, said Dr. Lowe, the medical student would find plenty of reputable company among materialists—those who plumped for the body and relegated the mind to the periphery, if not completely into limbo. All the same he wanted to suggest that they might well be a little hesitant before committing themselves in this direction. It was obvious that if all so-called thinking was merely the resultant of a chain of physical causation no validity whatever could be attributed to human judgment, and if man's freedom was a complete illusion it was not sensible to call any human action either good or bad. The most ardent theoretical materialist was seldom so consistent in his principles as to refrain from praise or blame for his fellows. He acted in practice as if he believed them free in some measure to choose, in spite of his professed conviction that they could not be free. Materialism in establishing its conclusion in effect destroyed itself.

Materialism and the Doctor

Turning to the day-to-day practice of the medical profession, what doctor did not constantly assume and act on the assumption that mental states and thoughts might and often did have physical complements? What physician did not regularly invoke the will power of his patient to work towards a cure? It was extraordinarily difficult to justify such procedures on a purely mechanistic hypothesis. The regular and approved practice of the medical profession in fact ruled out any theory which attempted to explain mind solely and completely in terms of bodily process. Scientific materialism was at variance with common sense and common practice, was in violent conflict with ethics and aesthetics, was insecurely based in physics, and was quite indefensible in logic.

He remarked upon the curious fact that while probably the great bulk of biologists and psychologists to-day adopted or tended towards the materialistic view, this was not nearly so true in the physical sciences. It was an extraordinary paradox that psychology should do its best to demonstrate that mind did not exist, while physics, the basic science of matter, was very far from accepting the standard of mechanical causation upon which materialists relied, and was in fact moving towards a position which was more closely akin to the idealism of Kant than any other type of philosophy.

In conclusion Dr. Lowe said that it looked as if they could not completely explain either the body or the mind in terms of the other. They must somehow hang on to the reality of both, and at least leave the way open for a philosophy of life which comprehended both. "I am convinced that you will not find anything in the work which you are starting to-day which precludes you from at least considering seriously the claims of such a view."

A vote of thanks to the Vice-Chancellor was moved by Professor R. J. V. Pulvertaft and seconded by Mr. D. Levi.

CHARING CROSS HOSPITAL

On October 5 the inaugural meeting of the Charing Cross Hospital Medical School for the new session was held for the first time at the Royal College of Physicians. Sir John Stewart Wallace was in the chair, and the prizes were bestowed by Lady Inman.

Lord Inman, in an address to the students, recalled the fact that it was just 30 years since he first entered the service of Charing Cross Hospital; it had been a happy and satisfying experience. He explained that he had intended to speak on changes which he would like to see in the National Health Service, but, owing to the impending general election, he refrained from taking that theme. He thought it a great pity that so vital a question as the health of the people should be the subject of party controversy. He desired to see it raised to a plane far above the party arena.

History of the Hospital

Instead of a subject which might be considered political he addressed himself to the history of Charing Cross Hospital. When the hospital was founded Charing Cross had a dense and poverty-stricken population. In Wild Court, near what was now Kingsway, 1,000 people had lived in 13 houses. It was to help such people that Dr. Benjamin Golding, with a friend, John Robertson, who became the first secretary of Charing Cross Hospital, had started the West London Infirmary. In order to provide also in-patient treatment, he took a house in Villiers Street, where 12 patients could be accommodated, and then set out to raise £20,000 to build a hospital. He encountered opposition. The *Morning Herald* suggested a lunatic asylum for those who wanted to build a hospital on land set aside for improvements. After long negotiations with the Department of Woods and Forests a site was granted, and the foundation stone was laid by the Duke of Sussex in 1831. By the terms

of the charter of the new hospital no salary was to be paid to any medical officer until the funds of the institution were sufficient to warrant it. The charter also provided for domiciliary attendance for those too ill to come to hospital, and for money gifts—not to be more than five shillings at a time or a guinea in all—for the purchase of extras to assist recovery. Every medical officer had to sign a declaration promising to conduct himself with openness and goodwill towards his professional colleagues and all other officers.

At the time Dr. Golding died, in 1863, 370,000 patients had been treated, and the hospital was free from debt and had accumulated and invested over £30,000—truly a remarkable achievement.

The Dean of the School, Dr. E. C. Warner, stated in his report that in October, 1952, preclinical students would be taught at the Royal Veterinary College under teachers from the Medical School. During the session 1950–1 there had been 135 students in the clinical years at the school.

Plans for the new Charing Cross Hospital and Medical School at Northwick Park were on view at the meeting.

Nova et Vetera

JENNER

The modern method of recording the events of the life of a scientific man in terms of his actual achievements—normally expressed in printed books or articles—is an immense advance on the old method of providing a mere list of his works, bibliographically set forth. Bibliography is an indispensable medium for every sort of scientific work, but for the high lights of science, its greater creative figures, it is now effectively replaced by bio-bibliography. Mr. LeFanu gives us here a model for the technique of this relatively new approach.[1] With Mr. LeFanu's book Jenner descends from the clouds of hero-worship and becomes a credible and intelligible human being, who walked the earth and had his recreations and even his weaknesses, much as we all do and have. For truly the great figures of science were neither saints nor gods, but just men with a touch here and there of something that other men have not. The light of genius is, at best, but fitful.

The method of bio-bibliography, when it has been adequately applied to a large enough number of these great men, may have something to tell us about the nature and nurture of the scientific spirit. If and when these conditions are recognized, we may learn how to select and cherish the happy carriers of the illuminant of genius. In this sense bio-bibliography may become the most practical of all social studies.

Mr. LeFanu is in a peculiarly favourable position for undertaking his task. As curator of the great library of the Royal College of Surgeons of England, he has charge of a large number of Jenner relics. That library is indeed replete with memories of Jenner, for he was the favoured pupil of John Hunter, and his work was, from the first, inspired by his mighty master. At the same time the task of Mr. LeFanu has been specially difficult in that much of his bio-bibliography has had to do with manuscripts, and these are more refractory of bibliographical treatment than are printed books. Moreover, the manuscripts themselves are scattered through many other collections. Mr. LeFanu has doubtless drawn many coverts that were blank and are therefore not recorded by him, but he does tell of the results of his investigations extended to more than 80 libraries. The amount of labour, of correspondence, and of ordering of the finds that such a research entails must have been enormous. Mr. LeFanu and the library that he adorns have to be congratulated on this admirable achievement, which, unlike many efforts of the kind, is in large part highly readable.

Charles Singer.

[1] *A Bio-bibliography of Edward Jenner (1749–1823).* By W. R. LeFanu. (Pp 176; 28 illustrations. £4 4s.) London: Harvey and Blythe. 1951.

Correspondence

R.M.B.F. Christmas Appeal

Sir,—I appeal to members of the medical profession, whether subscribers or not, to send donations to the Christmas Gifts Fund for beneficiaries of the Royal Medical Benevolent Fund.

The committee generally tries to send a present of £5 to each beneficiary. I therefore hope that there will be a generous response to this appeal. Christmas gifts have a very deep and special significance, for they make the beneficiaries realize that they are being remembered by their more fortunate colleagues. In the present difficult times Christmas gifts are more urgently needed than ever before. Contributions should be sent to the secretary of the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, and marked "Christmas Gifts."—I am, etc.,

Webb-Johnson,
President, Royal Medical Benevolent Fund.

Putney, S.W.15.

College of General Practice

Sir,—There is a College of Physicians, a College of Surgeons, a College of Obstetricians and Gynaecologists, a College of Nursing, a College of Midwives, and a College of Veterinary Surgeons, all of them Royal Colleges; there is a College of Speech Therapists and a College of Physical Education, but there is no college or academic body to represent primarily the interests of the largest group of medical personnel in this country—the 20,000 general practitioners. Many practitioners sadly felt the lack of such a body when negotiations about the National Health Service were taking place.

Preliminary discussions are now being held in the General Practice Review Committee of the British Medical Association about the possible development of such a College of General Practice, to help practitioners in the same ways that the Royal Colleges have helped their own Fellows. Such a proposal must not interfere at all with the present qualifying examinations or with the many other activities of the Royal Colleges. It should be able to help practitioners in a great many ways—by supervising their education and postgraduate work, by improving the standard and status of general practice, and by acting as a repository for its traditions—all at little or no cost to the taxpayer.

We are anxious to collect evidence upon this subject of a possible College of General Practice. If any of your readers have suggestions or comments to make, for or against this proposal, will they please communicate with us?—We are, etc.,

F. M. Rose,
99, Fylde Road, Preston, Lancs.
J. H. Hunt,
54, Sloane Street, London, S.W.1.

Injuries in Flying Accidents

Sir,—The post-mortem examination on the body of the pilot of the second ill-fated de Havilland 108 plane, which disintegrated in the air on February 15, 1950, showed traumatic rupture of the aorta as described by Dr. Donald Teare in his article on "Post-mortem Examinations on Aircrash Victims" (September 22, p. 707). In this case the aorta, throughout its course and including the common iliacs, was segmented, each segment corresponding to a vertebral body, the vertebral column having completely "sprung." The calculated disintegration force lay between 30 and 40 *g*. When found the pilot was still strapped to his seat by his safety belt. In the case of the aeroplane which crashed at Sywell Aerodrome, Sywell, Northants, on June 13, 1948, the accident was caused through the pilot, aged 45, having suffered an anginal attack. On post-mortem examination

the ascending part of the aorta showed several incision-like transverse intimal slits, a finding noted in several other instances of sudden death, but no rupture proper.

In another instance a form of traumatic rupture of the aorta has been seen on post-mortem examination of an elderly rider in a point-to-point race where the going was hard and the meal previously enjoyed a most hearty one. In the case of people suddenly buried by sand no traumatic rupture of the aorta has been noted, due to the equalization of the pressure applied. It is obvious, therefore, that traumatic rupture of the aorta occurs through the sudden application of an external force either to the abdominal or to the thoracic regions; and, if one thinks that in a rough sea the closer one can get one's back to a strong bulkhead the better, so too, in aircraft travel, as Dr. Teare puts it, with one's "back to the engine" this risk would be minimized.—I am, etc.,

Northampton. R. M. HEGGIE.

SIR,—Dr. Donald Teare's most interesting article (September 22, p. 707) concerning the post-mortem findings on the victims of a recent air crash omits one interesting and important point which he may care to elucidate—namely, the nature and position of the injuries in the 10 cases of fractured skull. If a passenger facing forwards is suddenly hurled against a bulkhead or the back of the seat in front, he will in all probability have a penetrating fracture of the front of the skull. If, however, he were facing backwards and the seat did not remain fixed to the floor under the deceleration stresses imposed it is probable that the result would be a fractured base. It would be interesting to hear Dr. Teare's findings in these cases.—I am, etc.,

Bristol. K. G. BERGIN.

Examining the Dead

SIR,—I am afraid judgment has been hard in the case of the doctor who pronounced dead a young woman who afterwards was found to have been strangled (September 15, p. 662). I believe the doctor's conduct was quite correct. Having found a stranger to him dead, he very properly reported the case to the coroner, whose duty it was to find the cause of the reported death. Had the doctor pursued an investigation on his own initiative he might have laid himself open to severe censure by authority. This has happened before.

As a doctor of 40 years' practice I would not rely solely on the stethoscope. I would put the eye examination first and the stethoscope second. A dead eye is, to my mind, unmistakable. Yet when a man died suddenly some years ago almost at my feet from angina, all the signs of death were present, but the carotid on one side (the left, I believe) still beat for a minute or two intermittently. This was witnessed by several people, one of whom I know to be living.—I am, etc.,

Shrewsbury. ALBERT E. NICHOLLS.

Coma Due to Acidosis

SIR,—The following case of coma due to acidosis is similar, in many respects, to the one reported by Dr. C. B. S. Fuller (September 15, p. 652).

On two occasions this healthy boy of 8 years has been in hospital in coma, apparently due to acute acidosis. On the first occasion, on September 26, 1946 (the child was then 3 years old), he was admitted to hospital in coma with vomiting and acute acidosis. His blood sugar was normal, and his urine was full of acetone. He made an uneventful recovery, and was discharged from hospital on October 11.

On September 3, 1951, he was again admitted to hospital with a history that for 24 hours he had vomited continuously and had gradually become drowsy, being comatose before admission. He was unconscious, and vomiting almost continuously small amounts of bile-stained mucus. There was considerable salivation, and the child smelt strongly of acetone. No abnormal physical signs were found, and the blood sugar was 60 mg. %.

A diagnosis of coma due to acute ketosis was made, and the stomach was washed out through a Ryle's tube with bicarbonate of soda, intravenous dextrose being given. Within a few hours the child was improving steadily, and was able to take glucose drinks. On September 4 he was still drowsy, but the urine was gradually clearing, and the patient was discharged from hospital on September 11, having made a complete recovery.

I should be grateful to know if other cases have been observed, as I have not previously seen acute ketosis uncomplicated by diabetes produce coma.—I am, etc.,

Barnstaple. R. M. J. HARPER.

March Fracture in Childhood

SIR,—I should like to reply to the letter of Dr. A. L. Griffiths (September 15, p. 675) in which I am quoted as having stated that stress fracture of the metatarsals was rare in childhood. This was not the impression I intended to convey. I believed I had made this clear in the opening sentence of my memorandum, which stated that the diagnosis was rarely made in childhood. In the original manuscript, which was later condensed for publication, I put forward suggestions for this apparent rarity. These impressions are similar to those of Dr. Griffiths. Several of my colleagues in general practice have confirmed my belief that since the initial symptoms are so transitory these cases are frequently treated at home, thus excluding the possibility of an *x*-ray diagnosis. I should also like to add that since publication of the article a further case of such a fracture, confirmed by *x*-ray examination, has been seen at this hospital.—I am, etc.,

Glasgow. D. A. MACPHERSON.

Collapse after "Ethamolin"

SIR,—Mr. J. A. Rhind, in his paper on the "Injection Treatment of Hydroceles and Spermatoceles" (September 22, p. 711), does not offer any explanation for the collapse of a few patients after injection with "ethamolin." Might it not have been that these were cases of congenital hydrocele in which ethamolin had been inadvertently injected into the peritoneal cavity? It seems that this complication might occur in such cases and could be dangerous. To be sure a patent processus vaginalis did not exist one would have to attempt to reduce the fluid, inject air, and screen for its subphrenic collection.—I am, etc.,

London, S.W.17. B. H. BURNE.

Blackwater Fever in African Children

SIR,—Having read with great interest Dr. D. B. Jelliffe's paper on blackwater fever in African children (May 19, p. 1117), I most emphatically disagree with its generalizations and with the author's exaggerated fears that occasional use of antimalarial drugs (not only quinine) in African households may be followed by an increased incidence of blackwater fever due to the subsequent "inability to build up an effective immunity against the parasite." The problem of effects of treatment on the development and degree of immunity acquired against malaria is by no means simple. Dr. Jelliffe's warning rests on evidence too slender to form a basis for a public health policy.

Sinton (*Acta Conventus Tertii de Malariae Morbis*, Amsterdam, 1938, **2**, 312), in one of the most important contributions to the study of effects of treatment upon immunity, concludes that in populations where the chances of reinfection are comparatively slight the treatment adopted should aim at a radical cure of infection, but if the individual is exposed to multiple reinfections with many species and strains of the malaria parasite attempts should be made to allow him to acquire immunity to the polyvalent malaria infection. To achieve this the mere clinical treatment of attacks of the disease would be sufficient, since a prolonged stimulation of a low-grade parasitaemia would supply small amounts of antigen over a considerable period, and would eventually lead to a high degree of acquired immunity.

On the other hand a prolonged specific treatment of a large community living within a highly endemic area may eventually

decrease the collective immunity so that severe outbreaks will occur when massive reinfection takes place. As the presence of trophozoites assures the persistence of immunity the continued application of suppressive (=prophylactic) drugs may also prevent the development of immunity or increase the rate at which it is lost. Consequently, if the possibility of reinfection is not entirely eliminated serious reactions may occur (Findlay, *Recent Advances in Chemotherapy*, 1951, 2, 121). (This is what apparently happened when in 1936 Komp and Clark used intensive mass treatment in a highly endemic area in Panama.)

Few malariologists would disagree with the opinions quoted above. As it is, few of them would accept a recommendation that an African child continuously exposed to infection should be given from its early infancy either a continuous uninterrupted chemoprophylactic regimen, which will have to be administered throughout life, or no antimalarial drugs at all, if a continuous exposure to infection is to produce an acquired immunity. These attitudes represent two extremes, of which the first is unattainable and the second impracticable and occasionally dangerous. Contrary to the opinion expressed by Dr. Jelliffe, the only practical plan is that of administration to African children, whenever necessity arises, of an adequate dose of a chemotherapeutic drug which will help the growing organism to withstand the often excessive load imposed by high parasitaemia (not necessarily associated with severe clinical symptoms) without thereby hampering the progressive building up of individual immunity against malaria. Whether administration to African children of quinine in particular would lead to an increased incidence of blackwater fever I am unable to predict. This is actually beside the point, since Dr. Jelliffe's argument was of a general nature and referred to all antimalarial drugs. Any doubts whether Nigeria is within the hyper- and holo-endemic area and any complaints of lack of relevant statistical data will be dispelled on reading the *Proceedings of the World Health Organization Malaria Conference in Equatorial Africa* (W.H.O. Technical Report Series, No. 38) held in 1950 at Kampala (Uganda).—I am, etc.,

Lagos, Nigeria. LEONARD J. BRUCE-CHWATT.

Clean Catheterization

SIR,—I was most interested to read Mr. Edric F. Wilson's description of a technique for clean catheterization (September 1, p. 529), particularly in regard to the sterile catheter jelly, which should fulfil an important need. There is one point in the technique which I feel can be simplified, and that is in the introduction of the lubricant jelly or surface analgesic. (I have personally used for the past ten years a combined analgesic lubricant: cocain. hydrochlor. 3.5%, sod. bicarb. 0.5%, tragacanth mucilage 50%, *p*-hydroxybenzoic ester 0.16%.) A ball-ended needle, designed originally for injection down the vein in the Trendelenburg operation, is used. The ball of the needle is smeared with the analgesic lubricant and passed down into the posterior urethra. This is done without any discomfort, and 5 ml. analgesic lubricant is then injected. The viscosity of the preparation is such that very little regurgitation occurs, thus eliminating the necessity and discomfort of a penile clamp. In the presence of increased sensitivity of an inflamed posterior urethra or trigone, it is an additional advantage to inject 2 ml. of a solution of cocaine hydrochlor. 4% with the ball end of the needle well in the posterior urethra, and this is followed by the usual injection of analgesic lubricant. This little modification in technique works like a charm in the familiar case of the frightened old man admitted to hospital with retention of urine, failed catheterization, and bleeding from the urethra.

I once heard it said by an eminent urologist that the first important step in technical urology was to learn the art of painless instrumentation. Although nothing can replace skill in passing the instrument, I submit that the injection of an effective analgesic lubricant into the posterior urethra in this way is a most valuable ally.—I am, etc.,

Ballater, Aberdeenshire. D. LANG STEVENSON.

Changes in Sweating after Prickly Heat

SIR,—The opportunity of investigating the reactions to heat of a newcomer to the Tropics, before and after suffering from prickly heat, does not often present itself. One can therefore understand Dr. W. S. S. Ladell's desire to report his single case (June 16, p. 1358), but the results of one experiment on one man should not be used for drawing general conclusions. It is well known that there are wide variations in the sweat loss and rectal temperature on exposure to identical climatic conditions, not only between different persons, but in the same person from time to time.

The presentation of the results further invites criticism. Instead of tables of values, there are given in Fig. 1 of Dr. Ladell's paper two bi-variant graphs. Comparison between them is difficult, as they do not have any points in common in any one direction. When he says, "He sweats more at a given rectal temperature," he presumably compares such points as (1) "After" and (4) "Before." It is to be questioned whether the values for the subjects at (1) in one experiment (on entry) can be compared with the values at (4) in another experiment (after 30 minutes in the hot room).

If measurements were made on entry, and at 10-minute intervals thereafter for the subject's stay of 100 minutes in the hot room, 11 sets of readings are available. These account for the 11 points on the graphs in Fig. 1. Therefore (1) must represent his point of entry at zero time; but at zero time he cannot have a sweat loss, whereas he is shown to be losing sweat at the rate of approximately 2.3 g./min. on one occasion and at 6.7 g./min. on the other. Further, we deduce from paragraph 1, column 2, page 1359, that the temperatures shown at (1) on both graphs were not the temperatures on entry into the hot room. If it is desired to compare the results obtained on the two occasions, the values at (1) on the one occasion should be compared with (1) on the other, (2) with (2), (3) with (3), and so on. These represent the values obtained for corresponding treatments—namely, exposure to the same climate for the same time. If this is done by constructing a table of values from the graphs the results in the table are obtained.

Point No.	Rectal Temperature (° F.)			Sweat Rate (g./min.)		
	"Before"	"After"	Difference	"Before"	"After"	Difference
1	99·9	99·25	0·65	6·7	2·3	4·4
2	99·92	99·33	0·59	9·1	5·9	3·2
3	100·02	99·60	0·42	13·1	10·3	2·8
4	100·25	99·95	0·30	17·5	15·7	1·8
5	100·56	100·4	0·16	20·2	18·3	1·9
6	100·92	100·85	0·07	19·2	20·0	−0·8
7	101·25	101·30	−0·05	20·8	21·3	−0·5
8	101·6	101·72	−0·12	21·8	20·5	1·3
9	101·83	102·10	−0·27	18·8	20·0	−1·2
10	102·06	102·45	−0·39	18·6	19·6	−1·0
11	102·32	102·80	−0·48	19·9	19·2	0·7

It remains to be shown that the mean difference is significantly different from zero. Applying the formula

$$\text{"t"} = \frac{\bar{x} - E}{\sigma/\sqrt{n}}$$

where $\bar{x}$ is the mean difference, E the expected values (zero), σ the standard deviation of the differences, and n the number of values,

$$\text{"t" (sweat rate)} = \frac{1.1}{1.88/11} = 1.94,$$ which is not significant.

Similarly "t" (rectal temperature)=0.693, which, again, is not significant. In both cases "t" at the 5% level of significance is 2.23.

If we neglect the first part of the experiment, and consider only the last six values, so that the effect of the widely differing conditions on entry is diminished, the values are

"t" (sweat rate)=0.605
"t" (rectal temperature)=2.415

neither of which reaches the 5% level of significance ("t"=2.57).

The only possible conclusion is that there is no significant mean difference between "Before" and "After," in either the sweat rate or the rectal temperature, either over the whole of the experiment or over the latter half. Thus no change in either sweat rate or body temperature has been demonstrated, and, as Dr. Ladell points out, the relation between arm sweat chloride and total body sweat chloride values is still under discussion.—We are, etc.,

F. P. ELLIS.
R. K. MACPHERSON.

Medical Research Council,
Royal Naval Tropical Research Unit,
Singapore.

SIR,—Drs. F. P. Ellis and R. K. Macpherson have read more into my communication than I intended; they have also failed to appreciate the difference between a "period" and a "point" in time, hence their difficulties in assessing my Fig. 1. In my experience the comparison between the two sweat-rate/rectal-temperature curves is perfectly valid, as until an exposure has continued for 80 minutes or more the effect of time on sweat rate is small. I accept the result of their careful and ingenious statistical analysis, which shows that the sweat production of the subject was not significantly different between the two tests; but that there was no difference is in itself a subject for comment. The first time the subject was tested he had only recently arrived in the Tropics by air; the second test was made six months later after the hot season, during which the subject had from time to time indulged in strenuous exercise. Experience would therefore suggest that he should have shown some degree of acclimatization; and this, according to the consensus of physiological opinion, would be in increased sweating, a diminished temperature rise for a given task in a given climate, and a fall in the chloride content of the sweat from the arm or the whole body. But the subject showed, if anything, changes the reverse of this, or, statistically speaking, no significant changes at all. It was because of this apparent anomaly that I ventured to report the case, isolated though it was. As the subject had earlier complained of lassitude and debility, and had had severe prickly heat, he appeared to me to be similar in type, though not in degree, to those cases described by my colleagues and myself in Iraq as type II heat exhaustion.—I am, etc.,

W. S. S. LADELL.

Oshodi, near Lagos, Nigeria.

Discovery of the Formol Gel Reaction

SIR,—In the article "African Trypanosomiasis in a British Soldier" by Cates and McIlroy[1] it is stated, "The formol gel reaction was strongly positive (35 seconds)." In this connexion it may be of interest to call attention to the origin of this useful test for certain protozoal blood diseases in man and animals, which appears to have been overlooked in certain quarters.

1. While working with Gurkha troops in India in 1920 and early in 1921 I had under my care a batch of men returned from furlough in a kala-azar endemic area of Nepal. I was at that time trying out the Gaté and Papacostas (formol gel) reaction in syphilis, long since discredited in that disease. The result was my discovery of the quite different but highly characteristic reaction produced in the serum from cases of kala-azar. I published this hitherto unknown test in a brief note to the *British Medical Journal*,[2] wherein I further suggested that the test might also be strongly positive in trypanosomiasis.

After making my observations on a number of cases, I wrote to Knowles at the newly opened Calcutta School of Tropical Medicine (where many more cases were available) describing the new test in detail and asking him to confirm it. Knowles passed on my letter to Napier, who was working on kala-azar. Very shortly afterwards[3] it was announced that Napier had just discovered this new test, which was regarded as of great importance. (In fact, it is used to-day in India as a field test on vast numbers of kala-azar cases in rural endemic areas.) Napier, however, in his textbook on tropical diseases[4] specifically attaches his own name to the test and makes no mention whatever of my note.

2. While on active service in 1923 on the Indian Frontier I was able to follow up an idea mooted in my first article: I tested the reaction on surra, a most disabling trypanosome disease of camels, and I published the results in the *British Medical Journal*,[5] including a reference to my previous note in case it had been overlooked and expressing a hope that the test would be tried out in human trypanosomiasis, which does not occur in India.

For the reasons I gave the test has proved of very great value in camels, and now, according to Napier and others, it is routine in dealing with that animal; again he avoids mentioning that I discovered and described it. In this connexion further see G. Curasson, *Traité de Protozoologie vétérinaire et comparée*, 1943, 1, 47, Paris, where it incidentally appears that a French worker in North Africa applied the test to camels infected with surra at about the same time as I did in India, and with the same result. I do not know if he by chance was following up my original suggestion—probably not; and I may add that Mackie and Fox, working together in India in 1921, independently noted the characteristic behaviour of kala-azar serum to commercial formalin, but used a technique not now practised.

—I am, etc.,

W. C. SPACKMAN.

Limpsfield, Surrey.

REFERENCES

1 *British Medical Journal*, 1951, 2, 401.
2 Ibid., 1921, 2, 266.
3 Napier, L. E., *Indian med. Gaz.*, 1921, 338.
4 *The Principles and Practice of Tropical Medicine*, p. 164.
5 *British Medical Journal*, 1923, 2, 1257.

Diagnosis of Trypanosomiasis

SIR,—Our report of trypanosomiasis in a British soldier (August 18, p. 401) has prompted some interesting and instructive observations from those with experience of this disease. Several have stressed the diagnostic value of lymph-node puncture. Actually Professor Murgatroyd advised this procedure when he first saw the patient in 1948, but, as a second biopsy was also being planned, it was decided instead to make wet films of fluid expressed from this node when it was removed. These were negative.

Dr. H. L. Duke (September 15, p. 675), speaking from his wide experience, has explained why it is necessary to examine thick blood films as well as thin. In our case both thick and thin films were examined. However, in the end, the parasites were found in a thin film of the buffy coat. In our patient gross changes in plasma proteins and a positive formol gel reaction indicated that, although other investigations were negative, trypanosomiasis was still a possibility. It is therefore proper to mention that our attention has been drawn to Colonel W. C. Spackman's two papers 30 years ago in which he first described a positive formol gel reaction in both trypanosomiasis and kala azar.[1 2]—We are, etc.,

J. E. CATES.
M. B. MCILROY.

London, E.C.1.

REFERENCES

1 *British Medical Journal*, 1921, 2, 266.
2 Ibid., 1923, 2, 1257.

Proper Use of Insecticides

SIR,—The fact that application of an insecticide throughout a large area is likely in the course of a few years to result in the development of a high degree of resistance in the housefly *Musca domestica* was first demonstrated in Greece and Italy during malaria control operations with D.D.T. as a residual insecticide, and has since been confirmed all over the world. Subsequently it has been shown that this is not a peculiar feature of D.D.T. and that similar results will follow the use of benzene hexachloride (B.H.C.), chlordane, pyrethrins, etc., if these are used under the same conditions. It does not appear possible to avoid the development of fly resistance by the use of any single insecticide. This has induced several public health authorities to apply mixtures of insecticides—for example, D.D.T. and B.H.C. In some countries manufacturers are encouraging this approach to the problem by marketing such mixtures and advocating them for fly-control measures. The purpose of this letter is to point out that such action may well result in the development of fly strains resistant to both insecticides at once.

Although the investigations proceeding on the mechanism of the development of resistance are not yet complete there

is little doubt that genetic factors are concerned, and it can be taken that, when a fly population is subjected to a new factor inimical to the average in the environment, the more resistant members will survive, and the tendency will be to breed in the course of a few generations a new population with a higher proportion of resistant individuals. Evidence is now coming forward that this resistance factor is recessive, and if these flies are bred for several more generations without the presence of the adverse factor the proportion of non-resistant flies will steadily increase. This of course can happen only when the resistance developed is not complete, since breeding only from resistant flies would maintain the characteristic. Fortunately in the field it is most unlikely that fly-control operations would persist for such a time as to permit this to happen, and even if it did there would gradually develop from the perimeter of the area breeding with non-resistant flies. Even on an island like Sardinia introduction of flies by shipping provides considerable hope for ultimate reduction in resistance, though this may naturally be slower than where there is no sea barrier.

These remarks apply generally to any single insecticide, but the mechanisms of action of different insecticides are not identical: D.D.T.-resistant flies may have a normal susceptibility to B.H.C. Wherever, therefore, in the field there is any suspicion of fly resistance developing to D.D T. the treatment should be changed and B.H.C. substituted. Should B.H.C. have been used for initial operations the same argument holds, and alternation with D.D.T. is equally desirable. It may even be better to alternate these insecticides before any sign of resistance becomes apparent. This appears with our present knowledge to be a much safer procedure than the use of mixtures. Until such time as more research work has been carried out this recommendation and the reason for it should be widely known. So far only the house fly has been a serious problem, but it may not be impossible for mosquitoes to develop resistance at a slower rate, and if that occurred the present prospects of widespread eradication of malaria could rapidly recede. It is highly important, therefore, to utilize this phenomenon of fly resistance as an opportunity of discovering how best to obviate insect resistance in general.—I am, etc.,

I.C.I., Limited, Runcorn, Cheshire. F. P. Coyne.

Day Hospitals

Sir,—With reference to Dr. J. D. Sutherland's criticism (August 18, p. 404) of the pamphlet of this title, I should like to be permitted to stress the following points:

1. It is unfortunately true that through a series of misunderstandings between the author, the persons responsible for proof reading, and the publisher a number of errors in the text occurred, but these have been corrected in the edition which is now on sale.

2. The concept of a day hospital was evolved in this country without knowledge of any similar experiment in any other country. The term "day hospital" was first brought to my notice by Dr. Colman Kenton in 1949, but without any mention of its origin. Only in 1950 did I become aware that it had been used in psychiatry by Professor Ewen Cameron, a fact which I have acknowledged in my publication.

3. Dr. Sutherland emphasizes that in such a publication "there should be a concise statement of guiding ideas." This is just what this small pamphlet was intended to give. Instead of analysing these "guiding ideas" Dr. Sutherland discharges his duties as a critic by characterizing them as "vaguely conceived principles."

4. Dr. Sutherland finds it disconcerting that I have had to "drag in quite irrelevant pleas for a greater recognition of Adler's work." Neither he himself nor others, however, will be able to affect the increasing trend towards the fundamental ideas of Adlerian psychology which is clearly discernible in the development of modern psychotherapy and modern psycho-analysis. (See Alexander, Karen Horney, Sullivan, etc.)

5. It is so difficult for Dr. Sutherland to accept the idea that results can be achieved by methods shorter than those that he employs that he makes the daring and significant statement that such a claim is "of little help to psychiatry." To support the completely uneconomical method of long analysis which he uses he implies that it is justified in the treatment of "the psychoneurotic conflicts in the more intelligent sections of the community." It is reassuring to know that those responsible for the health of the people of this country do not entirely agree with Dr. Sutherland that short methods of psychotherapy and analysis are of little help in psychiatry.

6. I have often heard Dr. Sutherland using his favourite expression 'vested interests" in relation to established schools in medicine and psychiatry. Does he not realize that time has marched on, that psycho-analysis is no longer a revolutionary science fighting for recognition? It is now itself an established school with more "vested interests" than any other, in the form of methods and training. It is a pity that his power of analysis has not enabled him to see that in writing this criticism he has crossed to the other side of the fence.—I am, etc.,

London, N.W.3. J. Bierer.

Diagnostic Centres

Sir,—It is stressed over and over again by the consultants, who were our teachers in medical school, and by medical propaganda, that early diagnosis is of paramount importance. For example, we are told that all patients in the cancer age, presenting new and suspicious symptoms, should be investigated thoroughly with the least delay to exclude that dread condition.

No general practitioner has the facilities to carry out such investigations and he must therefore refer them to hospital. In most cases physical examination reveals nothing abnormal and it is essential that *x*-ray investigations, sigmoidoscopy, bronchoscopy, etc., be used to discover the early cancer or whatever disease is suspected.

Certain pathological investigations can be ordered by the general practitioner at the local district laboratory, and chest *x*-ray examinations can be done at the local chest clinic. Both of these institutions are usually extremely co-operative and rapidly return results to the G.P. These are all the investigations which a G.P. can control. If any other form of investigation is required he must refer his patients to a consultant at the out-patient department of a hospital. In most cases the consultant is also unable to find any physical abnormality and orders the investigations requested by the G.P. He is, in fact, "signposting" to the special departments of the hospital, in much the same way that G.P.s are decried for "signposting" to the hospital.

Letters to your *Journal* frequently state that the malingerer and neurotic should not be referred to hospital but should be urged to return to work. It was taught in my medical school that no patient should be labelled as "functional" until organic lesions had been excluded. Many so-called neurotics do have organic lesions and many others benefit by psychiatric treatment.

It would be of great service to G.P.s if they could order investigations of patients at diagnostic centres, which could be equipped with a laboratory and full *x*-ray apparatus. These centres, I suggest, are an immediate necessity and would be far less expensive to build and run than the health centres envisaged in the Act.

Consultants who have paid domiciliary visits to my patients have invariably asked for the patients to be admitted to hospital for investigation and treatment which cannot be carried out in the home or surgery. In my opinion the reason for the increased attendances at surgeries and at hospital out-patient departments is not due to the lowered standard of general practice in the eyes of the general public. It can largely be ascribed to the fact that more of the population can now afford to attend without the financial worry prevalent before the inception of the N.H.S.

I believe that a general practitioner is a specialist in minor ailments, who should know his limitations. He should be praised for detecting the patients needing specialist and hospital care. In fact he should be praised for "signposting" and not subjected to the abuse so evident in your correspondence columns. Personally, I would rather refer patients to hospital than treat the wrong condition at home.—I am, etc.,

London, W.11. DAVID SLOVICK.

Problems in Hospital Administration

SIR,—As chairman of the late Kingston Victoria Hospital and former (and original) member of the Kingston Group Hospital Management Committee, may I be allowed to comment on your leading article with the above heading (September 29, p. 782). You refer to the evidence given by the chairman of the South-west Metropolitan Regional Hospital Board before the Select Committee on Estimates and his saying "that the efficiency of the Service was suffering because people who were capable of doing the work well were disinclined to serve on boards and on hospital management committees." In the light of our experience at Kingston it would appear that those who are "capable of doing the work well" are those who are prepared to do exactly what they are told to do, with the uncritical efficiency of rubber stamps. During the Kingston dispute there were six members of the hospital management committee, including the chairman and myself, who opposed the conversion of this general-practitioner hospital to another purpose. Our opposition was constructive in that sensible and inexpensive alternatives were suggested. Not only were these alternatives turned down after little or no consideration, but in the course of two years each one of us was replaced by a more complacent substitute.

I was one of a deputation from the Kingston Group Hospital Management Committee to the regional board to discuss the Kingston Victoria dispute. During the discussion I ventured to suggest that policy should originate locally from bodies such as hospital management committees and be co-ordinated by regional boards. I was tersely informed by the chairman that as there were 52 groups in the region he could not be expected to deal with 52 policies. In the face of such an attitude and of the pernicious system of appointment from above rather than election from below, is it any wonder that intelligent men and women are reluctant to waste their time in futility?

It is not surprising therefore that the Select Committee itself commented that "local sentiment is by far the most powerful agency preventing the hospital service from degenerating into an arid bureaucracy."—I am, etc.,

South Croydon. N. SKENTELBERY.

Sulphamerazine Dangerous

SIR,—I read Dr. E. C. Atkinson's letter (September 15, p. 674) with enthusiastic interest. I agree with him in that I consider sulphamerazine is more dangerous than is generally believed. I had it administered to a boy of 5. The case was one of acute follicular tonsillitis. Very rapid recovery was followed by a "lucid interval" of 24 hours and then violent lower abdominal pain, vomiting, oliguria, and haematuria. I had prescribed 1 g. and then 0.5 g. six-hourly. In all 12 g. was administered—i.e., 3 oz. of the cream. He was admitted to hospital immediately, where he made a rapid recovery.

I feel that the domiciliary use of sulphamerazine is extremely dangerous, as a relatively large fluid intake is essential, and this cannot always be guaranteed even in the best-known households; and needless to say, human nature being what it is, this sulphonamide has not been used by me since I encountered this case. However, whatever our immediate feelings about cases of this type, one must endeavour to eliminate prejudice, depending as it does on an infinitesimal proportion of general medical experience throughout the country; so that the question still remains, How dangerous is sulphamerazine to children, and what is the incidence of complications? Should it be used in domiciliary practice?—I am, etc.,

London, S.W.16. W. BRAND.

Secrecy of Psychiatric Case Records

SIR,—It is a doctor's paramount duty to respect and safeguard the confidence of his patients. This is not merely an ethical tradition but a fundamental principle affecting treatment, therapeutic progress, and prognosis. In psychiatric cases particularly the extent to which the patient is satisfied that his case history and disclosures will remain confidential may materially influence the course of the illness. Under the National Health Service there has been a considerable increase in the number of clerks and secretaries employed in hospital out-patient departments who have access to case records. The intimate details of a psychiatric patient's life constitute the most interesting of all hospital notes to young lay employees, and it is by no means uncommon for confidential information to come into the possession of unauthorized persons.

It is too much to expect young people to overcome their curiosity regarding the particular ailment of a celebrity or to refrain from presenting "interesting" facts concerning patients to those whom they may wish to impress with the importance of their job. It is not too much, however, to expect the hospital authorities to take steps to prevent such breaches of confidence. It may be difficult under present hospital conditions adequately to safeguard the secrecy of case records, but it should be a comparatively simple matter to preserve the anonymity of the patient.

I urge the adoption of a system of numbering of patients, thus rendering it unnecessary to refer to them by name. The key could be in the custody of the psychiatric social worker on duty at any given time. It might be said that under such a system the patient will become merely a number, but perhaps that would be preferable to the risk of names being mentioned in some socially discreditable connexion.—I am, etc.,

London, W.1. ELLIS STUNGO.

Kingston Fund and the Law

SIR,—We have been greatly encouraged by the initial response to our appeal for the Kingston Victoria Fund. In the first three days of last week over a thousand doctors have subscribed and have written to us, many with expressions of goodwill which were profoundly moving. There is, however, one aspect of the case that has emerged from these letters which is somewhat disturbing, and that is the fear expressed by many that our Foundation may be nationalized in its turn and its moneys be appropriated by the State after the fashion of the Children's Ward Fund at East Grinstead. *Such in fact is not the case.* The Ministry of Health has no power under the National Health Service Act to acquire the funds of a charity such as ours founded after the "appointed day"—i.e., July 5, 1948. We have sought legal advice on this point and are assured that our funds could not be taken in the same way as the Children's Ward Fund at East Grinstead without a fresh Act of Parliament.—I am, etc.,

Kingston. F. B. LAKE.

POINTS FROM LETTERS

Ophthalmology at Oxford

Dr. FREDERICK SIMPSON (Perth, W. Australia) writes: I understand that the course for the D.O. (Oxon) has been discontinued. As one who has enjoyed this splendid course given by the élite of Britain's ophthalmologists, in the beautiful surroundings of the Isis, I hope that the decision will be changed. In the course I took there were present men and women from the five continents, and it was a wonderful education for all.

Obituary

P. G. McEVEDY, F.R.C.S.

J. M. writes: Peter McEvedy came to Manchester soon after the 1914–18 war as resident surgical officer at Ancoats Hospital. He brought excellent credentials from Guy's Hospital, where he had been house-surgeon to Arbuthnot Lane, but it caused a considerable sensation and much shaking of heads when at the end of his time as R.S.O. he was elected honorary surgeon to Ancoats Hospital against local candidates with a good deal more experience. The shrewd committee of management had not only assessed his ability, but preferred a man who would be likely to remain at Ancoats Hospital throughout his active surgical life, and not use it, as others had done, as a stepping-stone to the Royal Infirmary staff. McEvedy soon established a reputation as a surgeon of marked technical skill and originality of mind. Building up a consulting practice in his early days must have been difficult without local connexions, but there were Guy's men in practice in the district, and they never allow a good Guy's man to starve. Later he had additional appointments as surgeon to Warrington Infirmary and Stretford War Memorial Hospital, and his practice became a large one, but Ancoats always had the first place in his affection. He devoted great attention to those despised Cinderellas of surgery, varicose veins, piles, and hernia, and was one of the first to establish a special clinic for varicose veins and piles. His life-long enthusiasm for local analgesia accorded well with his delicate and light-handed operating and his love of a bloodless field. To watch his artistry in handling the tissues was an aesthetic treat, for he had a great delight in neat and dextrous technique, no doubt acquired from his master, Lane.

With all this he had a highly original mind and was a particularly inspiring postgraduate teacher. He instituted regular clinical meetings at Ancoats Hospital, which were attended largely by candidates for the F.R.C.S., and though all the staff combined to make these meetings a success McEvedy would always preside and was the life and soul of the party. "You must think pathologically," he would say, or "You must think anatomically." He was most kind and generous to his assistants, and many young surgeons owe much to his inspiration and encouragement during their time as his assistant. Although he always thought out his problems from first principles and was often highly critical of accepted doctrines, McEvedy was inclined to demand a full acceptance of his own teaching by his subordinates and a punctilious copying of his own technique. Doubtless he would have subscribed to Emerson's dictum, "Consistency is the hobgoblin of little minds." His work on the operative treatment of ulcerative colitis by colectomy was of a high order and led rather than followed surgical practice in this country.

Perhaps his outstanding characteristics were his moral courage and his humanity. His left-wing position in politics was determined by his constant sympathy for the underdog, and he rather enjoyed being in a minority among his professional brethren. For some years his health was impaired by a duodenal ulcer, but in spite of this he kept on steadily with his work, and after it had been cured surgically he had fifteen years of good health before his final brief illness. When investigation showed that his condition was beyond surgical or other curative treatment he faced the position with a calmness and courage that few could attain. In spite of increasing weakness he insisted on carrying on with some of his hospital work until a week or two before the end.

Dr. Joseph Drysdale Glaister, of Golspie, Sutherland, died suddenly on September 25, aged 55. He belonged to a well-known and distinguished Glasgow family. On demobilization after the 1914–18 war he studied medicine at Glasgow University, where he graduated M.B., Ch.B. in 1923. He then joined his father in practice in Glasgow, and continued after his father's death to run for many years a large and busy city practice. In 1943 he went to Sutherland and since that time had been in practice in Golspie and Rogart. He readily adapted himself to the wilder conditions of the North and soon became part of the people and the country. Of friendly and kindly disposition, active in the participation in the affairs of the community, skilled in his own profession, he soon became in Sutherland a man whose wise and considered opinion was often and never vainly sought. At the time of his death he was chairman of the Sutherland Division of the B.M.A., a professional member of the local executive council and many of its subcommittees, and member of the local medical committee. By his professional brethren he was held in the highest regard, and to his many friends and to the community at large his death will mean an irreparable loss. To his wife and three children still at school we extend our deepest sympathy.

Medico-Legal

ANOTHER MISSED PREGNANCY

[From Our Medico-Legal Correspondent]

A remarkable example of missed pregnancy came to light at an inquest held by the Brighton Coroner on April 27. Another case was described in the *Journal* of April 24 (p. 421). In November, 1950, Mrs. I. M. Noble, aged 22, visited a doctor at Croydon because of discomfort in the stomach, and according to her recollection was told she was suffering from gastritis and was given something to take for it. After seeing the doctor she felt better, and did not visit him again.

On April 14, 1951, Mrs. Noble came to Brighton with her husband to look for rooms, as her husband hoped to get work there, and on the evening of April 16 they went for a walk together to Rottingdean, some three miles away. On the way Mrs. Noble said she felt she had a stomach ache, but it passed off. On the way back the pain returned, and increased so much that she had to rest very frequently. After about a mile she could go no further, and her husband broke into a hut for shelter. While she was standing in the hut resting a female child weighing 5¾ lb. (2.6 kg.) was born. Mrs. Noble said that she had had no suspicion that she was going to have a baby. Her husband then went and fetched a nurse, who arrived within a few minutes and found the infant dead. Mrs. Noble was taken to Brighton General Hospital.

Dr. L. R. Janes, the pathologist who carried out the necropsy, found that death was due to pulmonary atelectasis and loss of blood immediately following birth. The cord had been torn off the infant at the umbilicus, together with the surrounding abdominal skin. The cord length was 29 in. (74 cm.), and the placenta was normal. Only the anterior parts of the lungs had been expanded by air. The tearing of the cord and surrounding skin was consistent with the child being born while the mother was standing up. The coroner entered a verdict that death was due to want of attention at birth.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending September 22 (No. 38).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending September 22					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	31	2	15	1	2	38	4	10	4	1	801	240	38
Deaths	—	—	—	—	—	1	—	—	—	—			
Dysentery	107	29	48	2		170	14	124	1	1	365	170	66
Deaths		—		—			—		—				
Encephalitis, acute	14	—	—	—		5	—	—	—	1	5	2	1
Deaths		—			—		—			—			
Erysipelas			12	2	8			21	4	6			
Food-poisoning	159	4		1		208	59		1				
Infective enteritis or diarrhoea under 2 years				23	64				10	26			
Deaths	5		2	3	1	14		2	2	1			
Measles*	1,069	41	90	96	94	2,673	201	97	41	32	3,375	1,208	397
Deaths		—	—	1	—		—	—	—	—			
Meningococcal infection	13	4	17	—		22	3	11	—	2	68	35	22
Deaths		—	1				—	—					
Ophthalmia neonatorum	21	1	14	—	2	37	4	3	1		112	69	36
Pneumonia, influenzal	281	13	2	3		260	13	4	—		459	312	226
Deaths (from influenza)†	5	—	—	1	—	5	—	2	—	—			
Pneumonia, primary			106					129	—				
Deaths	111	13		9	8	112	15		2	7			
Poliomyelitis, acute:													
Paralytic	48	3	11	4	2	419	24	51	9	5	594	50	10
Non-paralytic	37	2											
Deaths§	2	—			—	20	3			—			
Puerperal fever			10					6					
Puerperal pyrexia‖	246	32	3	—	1	72	4	8	1		166	115	72
Scarlet fever	621	51	179	41	45	771	52	134	49	53	2,792	1,097	805
Deaths		—	—	—	—		—	—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			135	34				157	35				
(2) Tuberculosis, non-respiratory			25	9				35	4				
(1) Deaths	116	18	17	3	6	118	18	22	3	15			
(2) Deaths		3	3	3	—		—	2	—	2			
Typhoid fever	10	—	—	1	2	3	1	—	—	2			
Deaths¶	—	—	—	—		—	—	—	—				
Paratyphoid fever	28	1	2 (B)	2	1 (B)	9	1	—	—		44	21	12
Whooping-cough	2,196	83	273	31	77	2,935	234	200	17	69	2,935	1,093	945
Deaths	1	—	—	—	—	1	—	—	—	—			
Deaths (0–1 year)	179	17	25	8	5	205	19	25	9	13	353	317	205
Deaths (excluding stillbirths)	3,736	557	483	92	123	3,880	596	534	104	154	4,123	3,838	3,554
Annual death rate (per 1,000 persons living)			9·9					10·7					
Live births	6,797	1,086	774	213	357	6,894	1,092	815	204	333	8,618	6,893	5,908
Annual rate per 1,000 persons living			15·9					16·4					
Stillbirths	175	24	17			181	35	29			266	191	169
Rate per 1,000 total births (including stillborn)			21					34					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Edinburgh in 1950

The infant mortality rate in Edinburgh in 1950 fell to 29 infant deaths per 1,000 live births, the lowest recorded figure for the city. In 1946 it was 52, and 10 years ago it was 68 (*Annual Report of the Public Health Department for 1950*). There was not a single death from diphtheria, scarlet fever, or measles.

The pulmonary tuberculosis death rate was the lowest in the city records—48 per 100,000 population; this was a fall of 12% from the previous year. The number of notifications was 681, which was 20 higher than in the previous year and the largest in the history of the city. It is mainly due to intensified searching for early cases.

Infectious diseases notified during the year numbered 7,209; this was 2,153 more than in the previous year and the largest total since 1945. Two main reasons for it were a measles epidemic in the spring and summer and the compulsory notification of whooping-cough from January 1, 1950. Three deaths from whooping-cough were recorded.

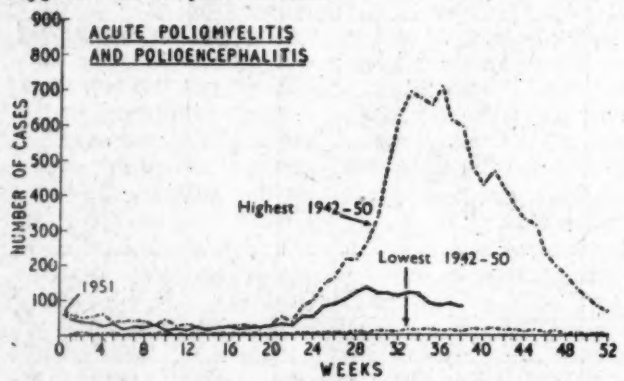
The general death rate of 12.6 per 1,000 population was much the same as in the preceding two years and slightly lower than it was in 1946 and 1947. In 1950, 10.4% of the population was aged 65 and over. In 1901 this group comprised 4.4% of the population.

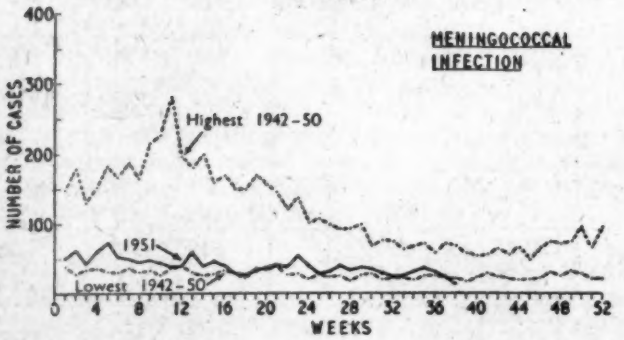
Week Ending September 29

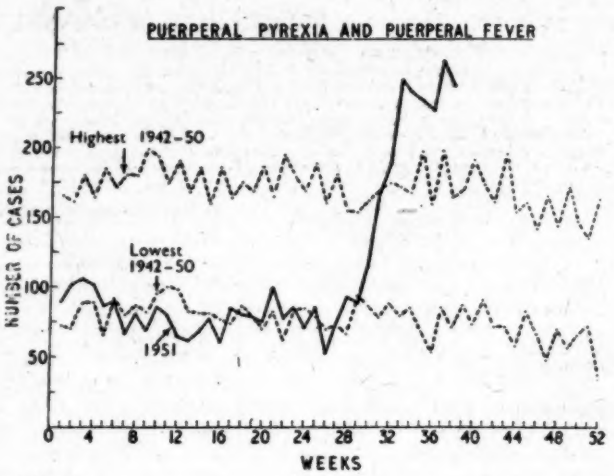
The notifications of infectious diseases in England and Wales during the week included: scarlet fever 741, whooping-cough 1,769, diphtheria 25, measles 1,258, acute pneumonia 258, acute poliomyelitis 108, dysentery 144, paratyphoid fever 33, and typhoid fever 5.

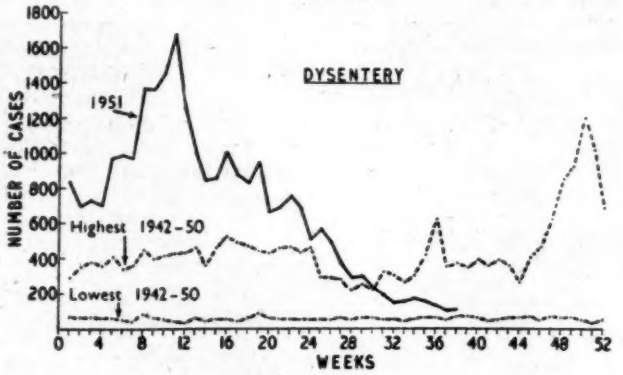
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

In England and Wales during the week ending September 22 a decrease was recorded in the number of notifications of whooping-cough 224 and measles 142, and an increase was reported for acute pneumonia 142.

No large variations occurred in the returns of measles. The decline was due to the experience of the southern section of the country; in the northern section a small rise was recorded. A small fall in the incidence of whooping-cough was recorded in most areas, and no large fluctuations occurred. The notifications of diphtheria were 5 fewer than in the preceding week. The largest changes in the local trends were a rise of 3 in Staffordshire and decreases in Warwickshire 5 and Lancashire 3. This is the first week that no case of diphtheria has been notified in Warwickshire. The notifications of scarlet fever were 26 more than in the previous week, but no change of any size occurred in the local returns.

The notifications of paratyphoid fever were the lowest for 10 weeks, and they were 10 less than in the preceding week. Eight further cases of paratyphoid were notified from the outbreak in Birmingham C.B., where cases have occurred for the past eight weeks.

The notifications of acute poliomyelitis were 5 fewer than in the preceding week. The largest centres of infection were Yorkshire West Riding 12 (Bradford C.B. 3), London 5, Warwickshire 5 (Coventry C.B. 3), Cheshire 4, Lancashire 4, and Wiltshire 4.

Four more cases of dysentery were notified than in the preceding week. The chief feature of the returns was an increase of 13 in Lancashire. The largest returns were London 29 and Lancashire 23 (Liverpool C.B. 14).

Poliomyelitis

Poliomyelitis notifications in the week ending September 29 were as follows (figures for the previous week in parentheses): paralytic, 64 (58); non-paralytic, 44 (37); total, 108 (85). The overall incidence of the disease in England and Wales to date is 5.02 per 100,000.

Medical News

Cortisone and the Eye

The November issue of the *British Journal of Ophthalmology* is to be devoted to the study of the value of cortisone and A.C.T.H. in ocular disease. Eight papers record the first results of clinical and laboratory studies carried out at the Institute of Ophthalmology, London. A preliminary assessment of the clinical value of these hormones in every type of ocular disease in which they have been tried is presented, with a summary of results so far reported in the literature. Details are then given of recent results in 416 cases in which the hormones have been administered locally.

Various members of the team of workers at the Institute of Ophthalmology discuss the action of cortisone on inflamed and damaged tissue in the eye, on corneal wounds in laboratory animals, on corneal vascularization following heat burns and damage by alloxan, on the permeability of the blood-aqueous barrier, and on tissue culture.

A limited number of copies of this special issue of the *British Journal of Ophthalmology* will be available to non-subscribers at 8s. including postage. They are urged to make early application to the Publishing Manager, *British Medical Journal*, B.M.A. House, Tavistock Square, London, W.C.1.

Future of the South Bank

Now that the South Bank Festival Exhibition has ended, schemes for the future use of the site are being announced. It is hoped that a "New Burlington House" on the river front facing Somerset House will form the new home of the Royal Society and 15 other leading scientific learned societies. Other buildings will house Government scientific organizations, including the Patent Office and its library, which will be modernized and extended as a first-rate central reference library of science and technology. Such a centre would be a valuable addition to the South Bank and would greatly improve facilities for, and contacts between, scientists and users of science, both nationally and internationally.

Hunterian Society's Annual Party

Once again the Society opened its season with an informal party at 41, Portland Place, W.1, where the Hunterian collection is now housed. Members and their wives and guests were received by Sir Arthur and Lady Porritt and Lord Horder. Sir Arthur, as president, later made a few remarks of welcome, in the course of which he mentioned that the Society's gold medal awards are now truly golden, and no longer the silver gilt substitutes of the war years.

Postgraduate Travelling Fellowships

The British Postgraduate Medical Federation (University of London) is prepared to offer a limited number of postgraduate travelling fellowships, tenable for one year, to registered medical practitioners who are in the course of training as specialists in one of the preclinical or clinical branches of medicine or surgery at one of the medical schools or teaching hospitals and postgraduate institutes of the University of London. Further information about these Fellowships will be found in our advertisement columns.

West London Medico-chirurgical Society

The triennial gold medal of this society, which is awarded for outstanding contributions in the field of medicine, was awarded to Dr. Charles Slocumb, of the Mayo Clinic, Rochester, U.S.A., at a dinner meeting held on October 5. The president, Mr. B. Sangster Simmonds, referred to the magnitude of the contribution made to medical science by the first announcement three years ago of the therapeutic activity of cortisone and A.C.T.H. by Drs. Hench, Slocumb, and Kendall. Dr. Slocumb gave an interesting paper outlining the steps which led to this discovery, summarizing the clinical experience of these hormones to date, and emphasizing their contraindications and dangers. A vote of thanks was proposed by Dr. W. S. C. Copeman, who briefly referred to the new conceptions of physiology and pathology opened out by these brilliant research tools, and Dr. Maurice Shaw seconded.

General Election Manifestos

According to the Liberal Party's manifesto "the social services must be safeguarded." The Communist Party's manifesto states that "our policy would also mean an end to the cuts and charges in the Health and Education Services and the full operation of the services promised in the Acts." Excerpts about the Health Service taken from the Conservative and Labour manifestos were given in these columns last week.

Emergency Bed Service: Applications and Admissions

During the seven days ending October 8 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 821, of which 89.64% were admitted.

COMING EVENTS

Lectures on Anaesthetics

The Faculty of Anaesthetists of the Royal College of Surgeons of England has arranged a course of lectures on anaesthetics to be given at the College (Lincoln's Inn Fields, London, W.C.) from Monday, October 15, to Friday, October 26, beginning at 10 a.m. each day. The admission fee for the whole course is £15 15s., or 10s. for one lecture. Admission cards may be obtained from Mr. W. F. Davis, Secretary, Faculty of Anaesthetists.

Twenty-seventh General Hospital Reunion

The fifth annual reunion of the 27th General Hospital will take place at the Eccleston Hotel, Eccleston Square, London, S.W.1 (near Victoria Station), on Saturday, October 27, at 6.15 p.m., for dinner at 7.15 p.m. Tickets £1, including wine. Colonel L. Haydon will preside. Inquiries should be addressed to Dr. L. S. Potter, B.M.A. House, Tavistock Square, London, W.C.1.

Maudsley Hospital Dinner

The first annual dinner for past and present members of the medical staffs of the Bethlem Royal and Maudsley Hospitals has been arranged for Thursday, November 8. Invitations have been sent out to all doctors who have held paid appointments at either hospital as far as can be ascertained. All those who feel entitled to an invitation but have not received it should communicate with Dr. D. A. Pond, Maudsley Hospital, Denmark Hill, S.E.5.

Manchester Medical Ball

The Manchester Medical Students Representative Council is organizing a ball to be held in the Whitworth Hall, University of Manchester, on November 2 from 8 p.m. to 2 a.m. (double ticket £1 1s.). Full information from the dance secretary, Medical School, Manchester, 13.

Scientific Films

The medical committee of the Scientific Film Association has organized a showing of films of interest to physicians at Guy's Hospital, London, on October 18 at 5.30 p.m. It is hoped to show the following films: "Foxgloves in Medicine"; "Tropical Sprue"; "Examination of the Cervical Lymph Nodes"; "A Case of Cerebellar Ataxia."

Marriage Guidance

A course of five lectures for postgraduates will be held at the London Marriage Guidance Council, 78, Duke Street, Grosvenor Square, W.1, on Wednesdays at 6 p.m. from November 7 to December 5. The fee for the course is £1 1s., and those wishing to attend should apply by letter to the secretary of the council at the above address by November 1.

Election Broadcast

Dr. Charles Hill has been chosen by the Conservative Party to give an Election broadcast at 9.15 p.m. on October 16.

Evaluation of Chemotherapeutic Substances

A symposium will be held at the Medical Society of London, Chandos Street, Cavendish Square, London, W.1, on October 26 at 2.30 p.m. and October 27 at 10 a.m. under the aegis of the Biological Methods Group of the Society of Public Analysts and Other Analytical Chemists. Friday will be devoted to antibiotics, antituberculous and antiviral substances and Saturday to antiprotozoal substances.

Worcester Service for Doctors

A special service has been arranged for doctors, nurses, and medical auxiliaries, and their wives, on St. Luke's Day, October 18, at 7.45 p.m. in St. John's Church, Worcester. The address will be given by Mr. Arnold Aldis on "The Missing Factor in Modern Medicine"; all are welcome, and will receive tickets on request from Mr. C. Martin Doyle, Cwm House, Castle Street, Worcester.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday

●POSTGRADUATE MEDICAL SCHOOL OF LONDON, Hammersmith Hospital, Ducane Road, W.—October 12, 4 p.m., *"Disorders Associated with Giving Intravenous Fluids,"* by Dr. D. Black.

Monday

HUNTERIAN SOCIETY.—At Talbot Restaurant, 64, London Wall, E.C., October 15, 7 for 7.30 p.m., dinner-meeting; *"Abreast of the Times,"* presidential address by Sir Arthur Porritt.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London, W.C.—October 15, 5 p.m., *"Poisoning by Fluorine Compounds,"* by Dr. Donald Hunter.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 15, 10 a.m., *"Disorders of Micturition in Nervous Disease and Kidney,"* by Mr. A. W. Badenoch; 11 a.m., *"Latent Syphilis and the Prognosis of Syphilis,"* by Dr. W. N. Mascall; 2 p.m., *"Congenital Anomalies of Bladder and Urethra,"* by Mr. J. E. Semple; 5 p.m., *"New Growths of the Bladder,"* by Mr. J. G. Sandrey At St. Peter's Hospital, Henrietta Street, London, W.C., October 15, 11.15 a.m., *"Transplantation of Ureters,"* demonstration by Mr. J. G. Sandrey; 3.15 p.m., museum demonstration, by Dr. C. E. Dukes.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, Keppel Street, Gower Street, London, W.C.—October 15, 5.15 p.m., *"Patrick Manson: The Father of Tropical Medicine (His Pioneer Work and its Influence on Modern Advances),"* Manson Lecture by Sir Philip Manson-Bahr.

LONDON UNIVERSITY.—At Guy's Hospital Medical School (Physiology Lecture Theatre), London Bridge, S.E., October 15, 5 p.m., *"Some Aspects of Caesarean Section,"* second of two special university lectures in medicine by Professor N. J. Eastman (Johns Hopkins University).

Tuesday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C., October 16, 5.30 p.m., *Nutritional Assessment of the Individual,"* by Professor J. Yudkin.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—October 16, 5.30 p.m., *"Blood Vessels of the Skin,"* by Dr. A. C. Dornhorst.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 16, 10 a.m., *"Calculous Disease and Foreign Bodies in Bladder and Urethra,"* by Mr. H. Rees; 11 a.m., *"Syphilis of Oral Cavity,"* by Dr. V. E. Lloyd; 11.15 a.m., *"New Growths of Bladder,"* by Mr. J. G. Sandrey; 2 p.m., ward round, by Mr. J. E. Semple; 3.15 p.m., demonstration of endoscopic instruments, by Mr. A. R. C. Higham; 5 p.m., *"Management of Acquired Fistula of the Bladder,"* by Mr. F. R. Kilpatrick.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—October 16, 5 p.m., *"Ophthalmic Injuries,"* by Mr. T. M. Tyrrell.

SOCIETY FOR THE STUDY OF ADDICTION.—At Medical Society of London, 11, Chandos Street, Cavendish Square, W., October 16, 4 p.m., *"Indications and Contraindications for Leucotomy in the Treatment of Alcoholism and Addiction,"* by Dr. Maurice Partridge. Discussion.

Wednesday

●DAVIDSON CLINIC, 58, Dalkeith Road, Edinburgh.—October 17, 8 p.m., *"Psychology and Law,"* by Mr. Paul Campbell, B.L.

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—October 17, 8 p.m., *"Optical Illusions,"* by Dr. John Primrose.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C., October 17, 5.30 p.m., *"Mycology—Structure and Classification of Fungi,"* by Dr. R. W. Riddell.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 17, 10 a.m., *"Swellings in the Scrotum, including Tumours,"* by Mr. J. D. Fergusson; 11 a.m., *"Eruptions Simulating Syphilis,"* by Dr H. Haber; 11.15 a.m., *"Injuries of the Bladder and Urethra,"* by Mr. A. R. C. Higham; 2 p.m., *"Hydronephrosis,"* by Mr. H. P. Winsbury-White; 3.15 p.m., museum demonstration, by Mr. D. I. Williams; 4.30 p.m., *"Indications for Treatment in Senile Enlargement of the Prostate,"* by Mr. F. J. F. Barrington.

LONDON UNIVERSITY.—At London School of Economics and Political Science, Houghton Street, Aldwych, W.C., October 17, 5 p.m., *"Technological Change and Human Relations,"* special university lecture in sociology by Professor Georges Friedmann (Paris). (See also October 19.)

●MINISTRY OF LABOUR AND NATIONAL SERVICE.—At Safety, Health, and Welfare Museum, Horseferry Road, Westminster, London, S.W., October 17, 3 p.m., *"The Employment of the Older Worker,"* by Sir Frederick Bartlett, F.R.S. (Tickets from Director of Public Relations of the Ministry, 8, St. James's Park, London, S.W.1.)

●POSTGRADUATE MEDICAL SCHOOL OF LONDON, Hammersmith Hospital, Ducane Road, W.—October 17, 3 p.m., *"Function-preserving Prophylaxis and Therapy in Pleural Effusion, with Special Reference to Pneumothorax Fluid,"* by Dr. Gosta Birath.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—October 17, 3.30 p.m., *"Eating and Sleeping Problems in Children"* (Illustrated), by Professor R. S. Illingworth.

SOCIETY OF CHEMICAL INDUSTRY: FOOD AND MICROBIOLOGY GROUPS.—Joint meeting with London and South-eastern Counties Section of Royal Institute of Chemistry at Chemical Society's Rooms, Burlington House, Piccadilly, London, W., October 17, 6.30 p.m., *"Bacterial Wastage in Eggs and its Control,"* by Mr. J. R. Vickery, Ph.D.

Thursday

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—October 18, 8.15 p.m., *"Some Aspects of Magnification in Radiography,"* by Dr. R. H. Herz; *"The Radiological Features of Rheumatoid Arthritis, with a Reference to the Enlargement Technique,"* by Dr. K. A. Rowley and Dr D. E. Fletcher.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C., October 18, 5.30 p.m., *"Nutritional Science and the Feeding of Populations,"* by Professor S. J. Cowell.

CHADWICK TRUST.—At English Theatre, Edmund Street, Birmingham, October 18, 4.30 p.m., *"Cholera and Sanitation in England,"* by Professor J. F. D. Shrewsbury.

EDINBURGH CLINICAL CLUB.—At B.M.A. Scottish House, 7, Drumsheugh Gardens, Edinburgh, October 18, 8 p.m., *"The Treatment of Hypertension,"* by Dr. J. G. M. Hamilton.

HONYMAN GILLESPIE LECTURE.—At University New Buildings (Anatomy Theatre) Teviot Place, Edinburgh, October 18, 5 p.m., *"Histamine: Its Actions and Fate in Man,"* by Dr. Henry Adam.

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—October 18, 5 p.m., *"Breast Feeding,"* by Dr. Charlotte Naish.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 18, 10 a.m., *"Incontinence in the Male; Atony of the Bladder; Enuresis,"* by Mr. D. I. Williams; 11 a.m., *"Medico-Legal Aspects of the Venereal Diseases,"* by Dr. W. N. Mascall; 2 p.m., *"Non-gonococcal Urethritis,"* by Dr. A. H. Harkness; 3.15 p.m., museum demonstration, by Mr. A. R. C. Higham. At St. Peter's Hospital, Henrietta Street, London, W.C., October 18, 11.15 a.m., ward round, by Mr. H. K. Vernon. At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., October 18, 5 p.m., *"Tests of Kidney Function,"* by Professor E. J. King.

LEEDS UNIVERSITY.—At University Union (Riley-Smith Hall), Leeds, October 18, 3 p.m., *"Unilateral and Subtotal Adrenalectomy in the Treatment of Hyperfunctioning Lesions of the Suprarenal Cortex,"* Moynihan Lecture by Dr. Waltman Walters. Members of medical profession welcome.

RENAL ASSOCIATION.—At Ciba Foundation, 41, Portland Place, London, W., October 18, 4.30 p.m., *"Alcohol and the Kidney,"* by Dr. M. G. Eggleton; *"Aberrant Renal Arteries and Hypertension,"* by Dr. A. G. Marshall; *"The Biochemical Origin of Some Renal Stones,"* by Dr. John Black.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—October 18, 3 p.m., *"The Development of Dermatology from the Time of Harvey,"* Harveian Oration by Sir Archibald Gray.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—October 18, 5 p.m., *"Tests of Kidney Function,"* urology lecture by Professor E. J. King.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—October 18, 5.30 p.m., "*Plastic Operations and Orbital Surgery*," by Miss Jean M. Dollar.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place London, W., October 18, 7.30 p.m., "*Schistosomiasis and Some of its Problems*," presidential address by Sir Neil Hamilton Fairley.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—October 18, 4.30 p.m., lecture-demonstration in neurology, by Dr. A. S. Paterson.

SOCIETY OF MEDICAL OFFICERS OF HEALTH.—At Tavistock House, Tavistock Square, London, W.C., October 18, 5.30 p.m., installation of Dr. W. G. Clark as president and delivery of presidential address

Friday

BIOCHEMICAL SOCIETY.—At London Hospital Medical College, London, E., October 19, 2 p.m., 301st meeting. Scientific papers will be read.

BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, London, W.—October 19, 5 p.m., meeting of medical members; 6.30 p.m., "*The Saturation Current at High Radiation Intensities*," by Mr. J. W. Boag, B.Sc.

EDINBURGH UNIVERSITY.—At Obstetrics Lecture Theatre, 60, George Square, Edinburgh, October 19, 5 p.m., "*Premature Rupture of the Membranes: Its Bearing on Maternal Febrility and Foetal Outcome*," Macarthur Postgraduate Lecture by Professor Nicholson J. Eastman (Johns Hopkins University, Baltimore).

FACULTY OF RADIOLOGISTS: DIAGNOSIS SECTION.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., October 19, 2.15 p.m., "*Paediatrics in Radiology—The Skull*," by Dr. J. Blair Hartley.

INSTITUTE OF CHILD HEALTH (University of London).—At Hospital for Sick Children, Great Ormond Street, London, W.C., October 19, 5 p.m., "*Obliterative Bronchitis and Bronchiectasis*," Alex. Simpson-Smith Lecture by Professor E. D. Churchill (Harvard University).

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—October 19, 5.30 p.m., "*Erythemas*," clinical demonstration by Dr. A. D. Porter.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 19, 10 a.m., "*Malignant Disease of the Prostate*," by Mr. J. D Fergusson; 11 a.m., "*Gonorrhoea*," by Dr. A. H. Harkness; 11.15 a.m., "*Stricture of the Urethra*," by Mr. J. E. Semple; 2 p.m., "*Anaesthesia in Urology*," by Dr. T. A. B. Harris; 3.15 p.m., demonstration of *x* rays, by Mr. F. R. Kilpatrick; 5 p.m., "*Infertility in the Male*," by Mr. A. R. C. Higham.

LONDON UNIVERSITY.—At London School of Economics and Political Science, Houghton Street, Aldwych, London, W.C., October 19, 5 p.m., "*Technological Change and Human Relations*," second university lecture in sociology by Professor Georges Friedmann (Paris). (See also October 17.)

●POSTGRADUATE MEDICAL SCHOOL OF LONDON, Hammersmith Hospital, Ducane Road, W.—October 19, 2 p.m., "*Joints and Synovial Fluid*," by Dr. D. V. Davies; 4 p.m., "*The Composition of the Body*," by Professor R. A. McCance, F.R.S.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh, October 19, 8 p.m., "*Facial Expression*," by Mr. R. Urquhart.

ROYAL SANITARY INSTITUTE.—At Stockport Town Hall, October 19, 10 a.m., "*The Prevention and Control of Infectious Diseases*," by Dr. J. Yule.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bedford.—On September 30, 1951, to Jean, wife of Dr. P. D. Bedford, M.R.C.P., Oxford, a son—Anthony Peter.

Gladwin.—On October 6, 1951, at High Wycombe, Bucks, to Dr. Barbara Gladwin (formerly Mulvaney), wife of Eric Gladwin, a son.

MARRIAGES

Alban-Jones—Lewys-Lloyd.—On September 8, 1951, at St. Mary's, Llanfair Caereinion, David J. A. Alban-Jones, T.D., M.R.C.S., L.R.C.P., to Delyth Lewys-Lloyd, B.A.

Martin—Bolam.—On October 4, 1951, at Upton Parish Church, Chester, Leonard Geoffrey Cadoux Martin, M.B., B.S., to Rosemary Janet Bolam.

Stock—Lunt.—On September 29, 1951, at Manchester, Stuart Stock, F.R.C.S.Ed., to Freda W. Lunt, M.B., D.C.H.

DEATHS

Alexander.—On October 3, 1951, at 3, Minster Road, Bromley, Kent, Douglas Reid Alexander, M.C., M.R.C.S., L.R.C.P., D.P.M.

Babington.—On September 27, 1951, Gladys Mary Joan Babington, M.B., B.S., of 24, Devonshire Gardens, Margate, aged 69.

Campbell.—On September 29, 1951, at 169, Commercial Street, Lerwick, Shetland Islands, James Campbell, M.B., Ch.B.

Carlton.—On October 3, 1951, Charles Hope Carlton, M.C., T.D., M.Ch., F.R.C.S., of 86, Brook Street, London, W., and 19, Westbury Road, London, N.

Carter.—On September 30, 1951, at 20, Sidmouth Avenue, Newcastle, Staffs, George Archibald Carter, F.R.C.S.Ed., aged 74.

De Boinville.—On October 3, 1951, at Smugglers Mead, Stourpaine, Dorset, Vivian Chastel De Boinville, M.D.

Griffiths.—On October 2, 1951, at Kidderminster, Worcs, John Crisp Griffiths, M.D., D.P.H., aged 80.

Jenkin.—On September 26 1951, at his home, Trimmers Field, Hindhead, Surrey, Nelson West Jenkin, M.B., B.Ch., aged 69.

McMillan.—On September 30, 1951, at Hove, James Clarke McMillan, M.B., B.Ch., D.P.H., of 20, Hurst Way, South Croydon, Surrey, aged 60.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Recurrent Angioneurotic Oedema

Q.—*What is the likely cause of, and what treatment is advised for, recurrent attacks of angioneurotic oedema affecting feet, face, or tongue in a man of 55? Attacks have been occurring for the last three years and are resistant to antihistamines, adrenaline, oral calcium, peptone injections, auto-haemotherapy, and sedation. The patient is otherwise in good health.*

A.—The most likely cause of recurring angioneurotic oedema in a man of 55 is sepsis. The teeth should be *x*-rayed to exclude apical infection, the antra and sinuses should be investigated, and the alimentary tract examined to exclude cholecystitis, appendicitis, and diverticulitis. In almost all cases, however, such septic foci are only one factor, and the nervous element of stress and strain is often more important. Histamine ionization is sometimes of value; a jelly or solution containing 1% histamine acid phosphate is ionized into the skin of the arm or leg until a headache or generalized flush is produced. This is repeated three times weekly on six or eight occasions. Most cases respond to antihistamines provided these are given in sufficiently big doses—that is to say, up to 800–1,000 mg. in 24 hours—but adrenaline in repeated doses is usually more efficient at the time of attacks.

What Makes Hair Grow?

Q.—*What factors influence the growth of human hair? Why do I have to shave off a greater length of beard than usual when I have been up for most of the night? How does the hair regulate itself to a constant length for different sexes and sites, and return to its normal after shaving or cropping?*

A.—Genetic factors determine the distribution of hair follicles, the innate character of hair and its colour, although some of these genetic factors may operate through the endocrine glands.

The growth of hair other than lanugo hair is influenced primarily by endocrine factors and particularly the oestrogen–androgen balance at birth, puberty, menopause, and in old age. Testosterone (androgen) stimulates the growth of the hair on the face, pubes, axilla, limbs, and body. Testosterone also increases the toughness, greasiness, and depth of colour of the scalp hair, as has been shown in the treatment of Simmonds's disease, but the effect of a prolonged excessive androgenic stimulus is to cause loss of scalp hair—for example, in Cushing's syndrome. Oestrogens favourably influence scalp hair. With thyroid deficiency there is loss of hair from the eyebrows and later from the body, and the scalp hair becomes thin and dry. Although thyroid will abolish these changes, a good deal of the effect can be achieved with other hormones, and it is possible that the thyroid acts via the adrenal glands. Other factors may secondarily influence the growth of hair, such as nervous and emotional, circulatory, nutritional, and toxic factors, as may trauma and radiation.

Certain dystrophies of hair growth, particularly one termed monilethrix, which is a familial inherited disorder, suggest that there is a periodic nocturnal and diurnal variation in growth. In monilethrix the hairs are regularly beaded, suggesting that during the period of sleep and rest there

is increased or diminished growth as compared with the active period of the day. This may explain the greater length of beard following a night of activity.

Hairs are cast at various intervals—from 18 months to six years—and are replaced by new hairs. A maximum length is peculiar to each hair, which grows back to just its original length after cutting. The rate of regrowth after cutting appears to vary with the age of the hair. A balance in the level of sebum on the skin surface is maintained in similar fashion, being restored rapidly after removal of surface grease. What exactly controls this natural maintenance of equilibrium is not known. It is, however, consistent with the knowledge that the stoutness and length of hair are not influenced by cutting and shaving, as is often feared by women suffering from hirsuties.

Transplantation of Bone Marrow

Q.—*Has bone containing marrow ever been successfully transplanted from a healthy donor to a patient suffering from a marrow disorder, such as aplastic anaemia? A surgeon has raised the possibility of this treatment in cases of Cooley's anaemia.*

A.—We have no record of this having been done, although there have been reports of unsuccessful attempts to transplant bone marrow. The basic difficulty in the failure to homograft tissues other than cornea and blood vessels is the development in the host of an actively acquired immunity against the particular tissue. Bone has been homografted in the past merely to serve as a strut and not to serve as a physiologically active unit. The technical problems involved in homografting bone containing bone marrow, with a view to red cell production, would be vast. For example, it would be necessary to ensure an adequate blood supply to the bone and its marrow. The problems would be even more complicated in Cooley's anaemia. In this anaemia, in addition to the basic familial defect, there is already hyperplasia of the bone marrow, and widespread structural changes in the bones, liver, and spleen. It is difficult to imagine a small amount of foreign bone marrow counteracting that clinical picture. In view of the familial defect in the red cell, homografting of bone marrow in an already enfeebled child would be a retrograde step from the experimental point of view.

Causes of Gingivitis

Q.—*How should a case of gingivitis (no obvious pyorrhoea or caries) be investigated and treated?*

A.—The causes of gingivitis are both local and general. Local causes include food stagnation, the wearing of dentures or appliances, rough or faulty fillings, lack of an adequately stimulating frictional diet, drying of the mucosa due to mouth-breathing, etc. General causes include disorders of the blood (e.g., leukaemias), vitamin deficiencies, deposition of heavy metals (e.g., mercury, bismuth), administration of certain drugs (e.g., phenytoin sodium), sometimes pregnancy. In many cases little obvious cause, save lack of adequate stimulation, can be found. Treatment will, of course, be founded on the diagnosis made.

Buccal and Ano-genital Syndrome

Q.—*A married man of 38, a clerk, has just had an attack of a burning sensation in the mouth with intense itching of the end of the penis and of the anus. In the mouth large snail-track ulcers appeared after 24–48 hours and healed in one week. No signs appeared in the anus, and the penis subsequently showed superficial ulceration, which may have been traumatic. He had a similar attack about two months ago, but has otherwise always been very healthy. Does this syndrome correspond to any clinical entity? What further investigations should be made? Can you suggest any prophylaxis or treatment?*

A.—The signs and symptoms described could be a mild manifestation of the muco-cutaneous symptom complex that occurs with erythema multiforme. This skin disease may be associated with buccal, anal, conjunctival, penile, urethral, and vulvo-vaginal lesions, and cases have been recorded in which mucous membrane lesions have occurred without involvement of the skin. With severe constitutional symptoms this type of disease is now known as Stevens–Johnson syndrome. Another closely allied syndrome (Behcet), in which involvement of the eyes is more severe, may be caused by the same infective agent. At present the cause of the disease is unknown: it may be due to a virus, especially as various workers have reported rapid cures with "aureomycin."

It is possible that the condition may be a drug eruption, and investigations should be carried out on these lines. Phenolphthalein, an ingredient of many proprietary laxatives, is frequently responsible. The two attacks in this patient were extremely mild, but, as with any ulceration on the genitalia, serological tests for syphilis should also be carried out.

Squirting Cucumbers

Q.—*The fruit of the squirting cucumber (Ecballium elaterium) is used in Cyprus as a folk remedy for jaundice. It is put in the nose and inhaled. We have recently had a patient who not only inhaled the vapour but also ingested a certain amount of the juice. Within four days he had developed a severe multiple peripheral neuritis. He was not suffering from jaundice but had some nausea and epigastric discomfort, which he thought might be an early stage of hepatitis. I have been informed that the squirting cucumber does contain a toxic substance and that elaterium, which was included in the B.P.C. of 1934, was obtained from this source. I should be glad to know if any cases of peripheral neuritis have been reported following ingestion of the juice.*

A.—There appear to be no references in the literature to the occurrence of peripheral neuritis following ingestion of the juice of the squirting cucumber. Elaterium is the dried sediment which deposits in the juice of the fruits of *Ecballium elaterium*. It is a powerful cathartic which is used in a dose up to ¼ gr. (32 mg.). It contains up to 30% of elaterin, which is the active ingredient and which is given in a dose up to 1/10 gr. (6.5 mg.). The use of elaterin is frequently followed by prostration, according to Sollmann, and 10 gr. (0.65 g.) may be fatal. Goodman and Gilman also speak of elaterin as intensely irritating, and say that an overdose leads to severe prostration. There is, however, no mention of peripheral neuritis.

Corrections

The authors of the paper entitled "Some Observations on Endogenous Cortisone Excretion in Man" (*Journal*, September 29, p. 762) wish to make acknowledgment to the Medical Research Council for a research grant given to Miss S. McCrae. They regret that through an oversight this acknowledgment was omitted from the original manuscript.

In the list of medical candidates who will be standing for Parliament at the General Election on October 25 (*Journal*, September 29, p. 793) we stated that Dr. Bernard Homa was honorary anaesthetist at the German Hospital, Dalston. Dr. Homa has told us that he no longer holds this appointment, but that he is a member of the London County Council, chairman of a divisional health committee, and a member of the board of governors of Charing Cross Hospital. During the last war he was a major in the R.A.M.C.

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